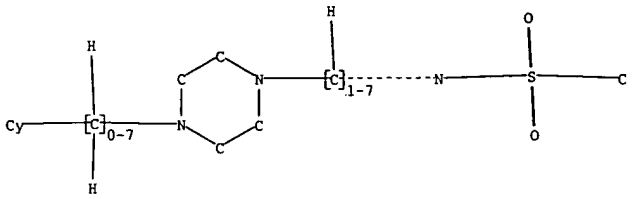
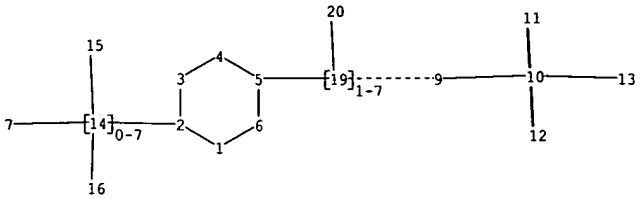
C:\Documents and Settings\EBernhardt\My Document



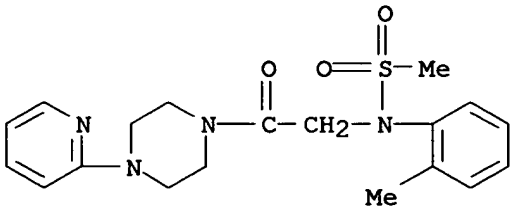




chain nodes :
7 10 11 12 14 15 16 20
ring nodes :
1 2 3 4 5 6
ring/chain nodes :
9 13 19
chain bonds :
2-14 5-19 7-14 9-10 9-19 10-11 10-12 10-13 14-15 14-16 19-20
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 2-3 2-14 3-4 4-5 5-6 5-19 7-14 9-10 9-19 10-11 10-12 10-13
exact bonds :
14-15 14-16 19-20

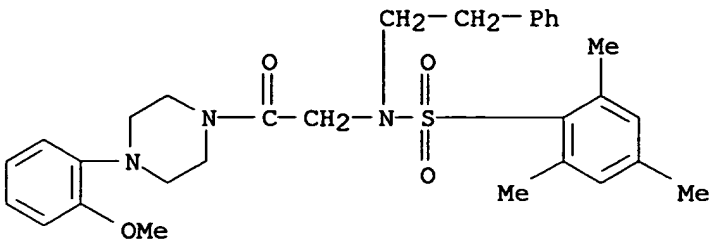
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 9:CLASS 10:CLASS 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 19:CLASS 20:CLASS
Generic attributes :
7:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System : Monocyclic

Element Count :
Node 7: Limited
O,O0
S,S0
N,N0-2

```
=> s l1
SAMPLE SEARCH INITIATED 19:26:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      359 TO ITERATE

100.0% PROCESSED      359 ITERATIONS                                  50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          6044 TO     8316
PROJECTED ANSWERS:             2003 TO     3397

L2            50 SEA SSS SAM L1

=> d l2 1 5 10

L2   ANSWER 1 OF 50  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   871558-73-5  REGISTRY
ED   Entered STN:  10 Jan 2006
CN   Piperazine, 1-[[(2-methylphenyl)(methylsulfonyl)amino]acetyl]-4-(2-
     pyridinyl)- (9CI)  (CA INDEX NAME)
FS   3D CONCORD
MF   C19 H24 N4 O3 S
SR   Chemical Library
       Supplier: Enamine
```

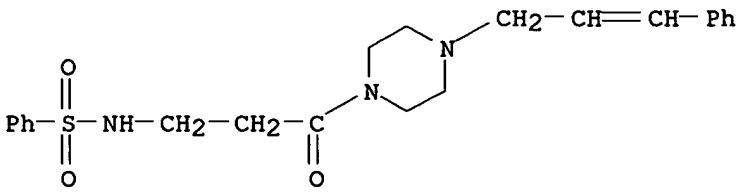



```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


L2   ANSWER 5 OF 50  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   867186-99-0  REGISTRY
ED   Entered STN:  10 Nov 2005
CN   Piperazine, 1-(2-methoxyphenyl)-4-[[(2-phenylethyl)[(2,4,6-
     trimethylphenyl)sulfonyl]amino]acetyl]- (9CI)  (CA INDEX NAME)
FS   3D CONCORD
MF   C30 H37 N3 O4 S
SR   Chemical Library
       Supplier: TimTec, Inc.
LC   STN Files:   CHEMCATS
```



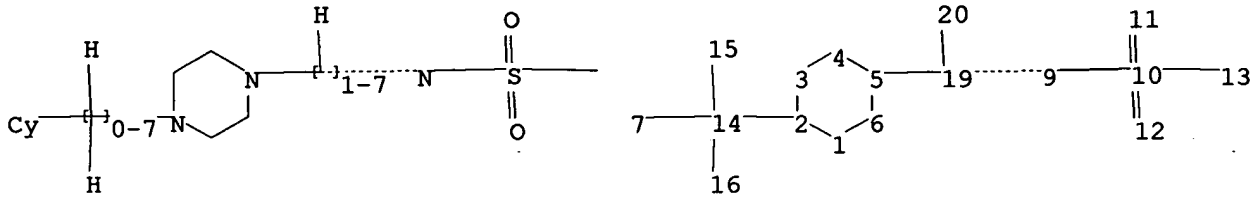
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L2 ANSWER 10 OF 50 REGISTRY COPYRIGHT 2006 ACS on STN
RN 850371-90-3 REGISTRY
ED Entered STN: 12 May 2005
CN Piperazine, 1-[1-oxo-3-[(phenylsulfonyl)amino]propyl]-4-(3-phenyl-2-propenyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H27 N3 O3 S
SR Chemical Library
Supplier: Enamine



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

=>
Uploading C:\Documents and Settings\EBernhardt\My Documents\Stnexp\Queries\Dhanoa-2.str



chain nodes :
7 10 11 12 14 15 16 20
ring nodes :
1 2 3 4 5 6

ring/chain nodes :
9 13 19
chain bonds :
2-14 5-19 7-14 9-10 9-19 10-11 10-12 10-13 14-15 14-16 19-20
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 2-3 2-14 3-4 4-5 5-6 5-19 7-14 9-10 9-19 10-11 10-12 10-13
exact bonds :
14-15 14-16 19-20

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 9:CLASS 10:CLASS 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 19:CLASS 20:CLASS
Generic attributes :
7:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System : Monocyclic

Element Count :
Node 7: Limited
O,O0
S,S0
N,N0-2

L3 STRUCTURE UPLOADED

=> s l3
SAMPLE SEARCH INITIATED 19:31:27 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 359 TO ITERATE

100.0% PROCESSED 359 ITERATIONS 24 ANSWERS
SEARCH TIME: 00.00.01

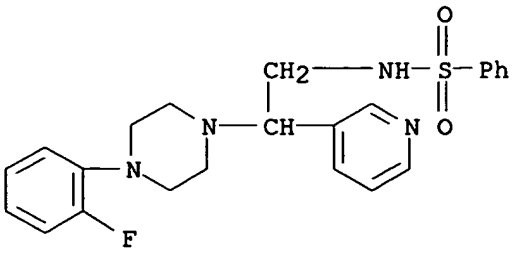
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 6044 TO 8316
PROJECTED ANSWERS: 187 TO 773

L4 24 SEA SSS SAM L3

=> d l4 1 5 10

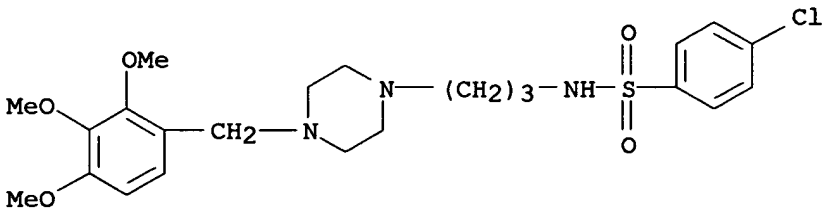
L4 ANSWER 1 OF 24 REGISTRY COPYRIGHT 2006 ACS on STN
RN 863586-88-3 REGISTRY
ED Entered STN: 21 Sep 2005
CN Benzenesulfonamide, N-[2-[4-(2-fluorophenyl)-1-piperazinyl]-2-(3-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H25 F N4 O2 S
SR Chemical Library

Supplier: Ambinter
LC STN Files: CHEMCATS

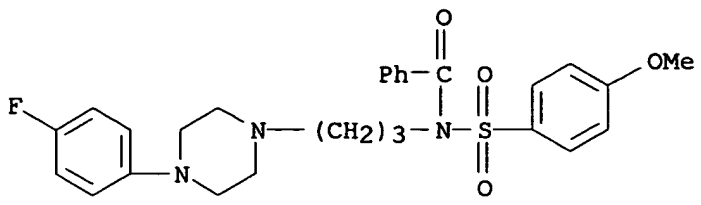


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

L4 ANSWER 5 OF 24 REGISTRY COPYRIGHT 2006 ACS on STN
RN 756441-87-9 REGISTRY
ED Entered STN: 03 Oct 2004
CN Benzenesulfonamide, 4-chloro-N-[3-[4-[(2,3,4-trimethoxyphenyl)methyl]-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H32 Cl N3 O5 S
CI COM
SR CA



L4 ANSWER 10 OF 24 REGISTRY COPYRIGHT 2006 ACS on STN
RN 169946-03-6 REGISTRY
ED Entered STN: 10 Nov 1995
CN Benzamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-N-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H30 F N3 O4 S
CI COM
SR CA
LC STN Files: CA, CAPLUS



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> s l3 sss full
FULL SEARCH INITIATED 19:31:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     8054 TO ITERATE

100.0% PROCESSED     8054 ITERATIONS                          551 ANSWERS
SEARCH TIME: 00.00.01

L5          551 SEA SSS FUL L3

=> save l5
ENTER NAME OR (END):ten768579/a
'TEN768579/A' IN USE
A single name cannot be used for two saved items at the same time.
Enter "Y" if you wish to replace the current saved name with a new
definition.  Enter "N" if the current saved definition must be
preserved.  You may then reenter the SAVE command with a different
saved name.  Enter "DISPLAY SAVED" at an arrow prompt (=>) to see a
list of your currently defined saved names.
REPLACE OLD DEFINITION? Y/(N):n

=> activate ten768579/a
L6              STR
L7          585 SEA FILE=REGISTRY SSS FUL L6

=> save l5
ENTER NAME OR (END):dhanoa/a
ANSWER SET L5 HAS BEEN SAVED AS 'DHANOA/A'

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               184.94     185.36

FILE 'CAPLUS' ENTERED AT 19:34:55 ON 27 JAN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
```

FILE COVERS 1907 - 27 Jan 2006 VOL 144 ISS 6
FILE LAST UPDATED: 26 Jan 2006 (20060126/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l5
L8 86 L5

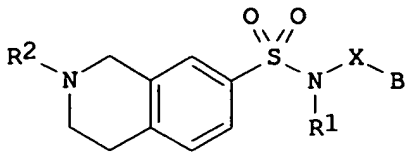
=> d l8 1-86 bib abs fhitstr

L8 ANSWER 1 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1260952 CAPLUS
DN 144:36263
TI Tetrahydroisoquinolylsulfonamide derivatives, their preparation and therapeutic use as H3 histamine receptor antagonists for the treatment of obesity, diabetes, and other conditions
IN Diaz Martin, Juan Antonio; Jimenez Bargueno, Maria Dolores
PA Sanofi-Synthelabo, Fr.
SO Fr. Demande, 31 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

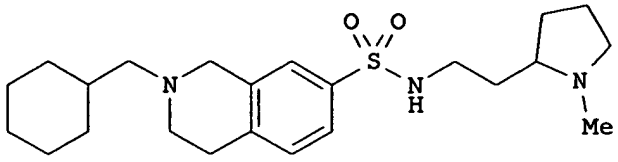
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | FR 2870846 | A1 | 20051202 | FR 2004-5607 | 20040525 |
| | WO 2005118547 | A1 | 20051215 | WO 2005-FR1279 | 20050524 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI FR 2004-5607 A 20040525
GI



I



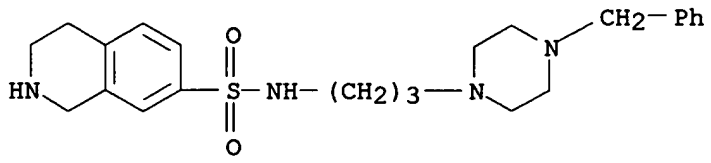
II

AB The invention concerns title compds. I [X = (Y)n; n = 1-6; Y = (un)substituted alkylidene; R1 = H, alkyl; R2 = H, cyclo/alkyl, etc.; B = NH2 and derivs.; (un)substituted pyrrolidin-2-yl, piperazin-1-yl, etc.] their acid addn. salts, hydrates and solvates. I are antagonists of histamine H3 receptors, and are useful therapeutically for the treatment of a wide variety of conditions, particularly obesity and diabetes. For instance, reacting N-[3-(diethylamino)propyl]-1,2,3,4-tetrahydroisoquinoline-7-sulfonamide (prepn. given) with cyclohexanecarboxaldehyde gave II in 62% yield. Compds. I bound to isolated rat brain H3 histamine receptors with Ki between 0.1 nM and 5.0 .mu.M. A feeding redn. assay in rats gave an AD50 of <10 mg/kg i.p. or p.o.

IT **870670-91-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of tetrahydroisoquinolylsulfonamide derivs. as H3 histamine receptor antagonists)

RN 870670-91-0 CAPLUS

CN 7-Isoquinolinesulfonamide, 1,2,3,4-tetrahydro-N-[3-[4-(phenylmethyl)-1-piperazinyl]propyl]-, hydrochloride (9CI) (CA INDEX NAME)

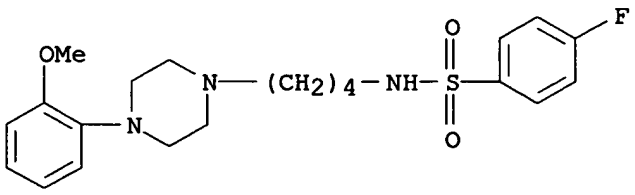


●x HCl

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1024934 CAPLUS

DN 143:460116
TI Synthesis and evaluation of 18F-labeled dopamine D3 receptor ligands as potential PET imaging agents
AU Hocke, Carsten; Prante, Olaf; Loeber, Stefan; Huebner, Harald; Gmeiner, Peter; Kuwert, Torsten
CS Department of Nuclear Medicine, Erlangen, D-91054, Germany
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(21), 4819-4823
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
AB A series of fluoro-substituted aryl carboxamides was synthesized revealing high affinity for the dopamine D3 receptor. In contrast to 2-methoxy substitution, a 2,3-dichloro substitution pattern at the phenylpiperazine moiety induces a 10-fold increase of D3 affinity which is expressed by Ki values of 0.53, 1.1, and 9.0 nM. Applying arom. 18F-for-Br(Cl) substitution, high radiochem. yields between 76-82% were obtained. The most promising ligand was used as imaging agent of the D3 receptor in vitro. However, due to the lack of specific binding, further studies should aim at the development of radioligands with improved D3 receptor selectivity.
IT **869383-35-7P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(calcd. LogP; prepn. of fluorine-18 piperazine aryl carboxamides as dopamine D3 receptor ligands for PET imaging)
RN 869383-35-7 CAPLUS
CN Benzenesulfonamide, 4-fluoro-N-[4-[4-(2-methoxyphenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)

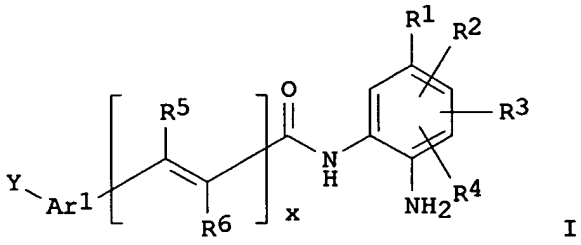



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

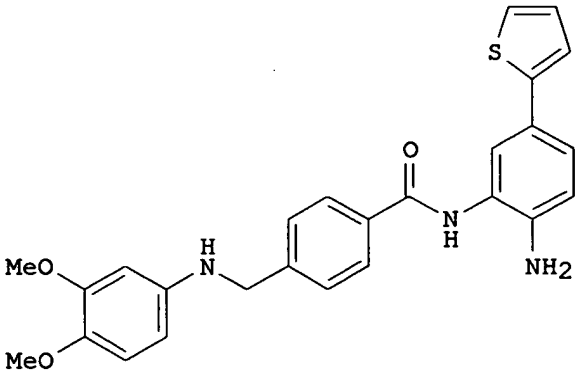
L8 ANSWER 3 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:300395 CAPLUS
DN 142:355054
TI Preparation of amide derivatives as inhibitors of histone deacetylase
IN Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PA Methylgene, Inc., Can.
SO PCT Int. Appl., 559 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

PI WO 2005030705 A1 20050407 WO 2004-US31591 20040924
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2003-505884P P 20030924
US 2003-532973P P 20031229
US 2004-561082P P 20040409
OS MARPAT 142:355054
GI



I



II

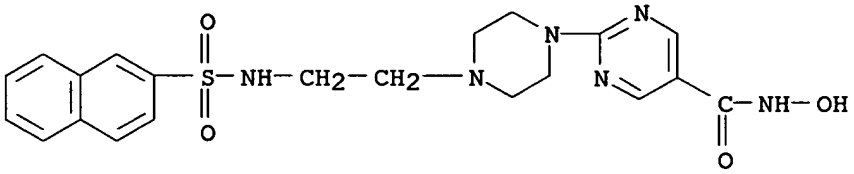
AB Title compds. I [Ar1 = (un)satd.-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally contg. 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chem. moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepd. and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepd. by Suzuki coupling of 2-bromo-2-nitro-phenylamine (prepn. given) with 2-thiopheneboronic acid

followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)-methyl]benzoic acid (prepn. given) and subsequent redn. The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 .mu.M. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

IT **603954-02-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amide derivs. as inhibitors of histone deacetylase)

RN 603954-02-5 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-[(2-naphthalenylsulfonyl)amino]ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

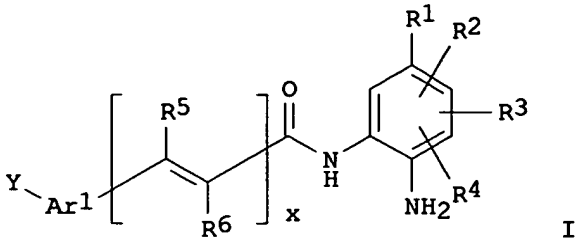


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

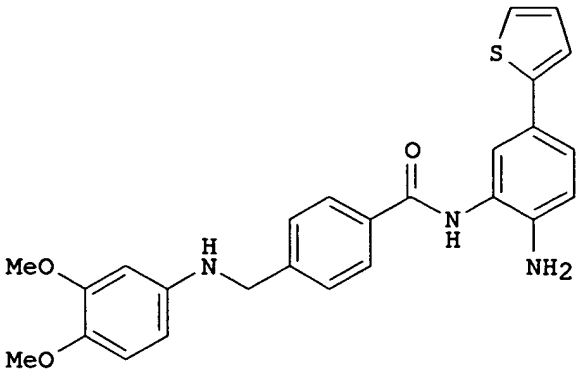
L8 ANSWER 4 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:300394 CAPLUS
DN 142:373563
TI Preparation of amide derivatives as inhibitors of histone deacetylase
IN Moradei, Oscar; Paquin, Isabelle; Leit, Silvana; Frechette, Sylvie; Vaisburg, Arkadii; Besterman, Jeffrey M.; Tessier, Pierre; Mallais, Tammy C.
PA Methylgene, Inc., Can.
SO PCT Int. Appl., 389 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2005030704 | A1 | 20050407 | WO 2004-US31590 | 20040924 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI | US 2003-505884P | P | 20030924 | | |

US 2003-532973P P 20031229
US 2004-561082P P 20040409
OS MARPAT 142:373563
GI



I

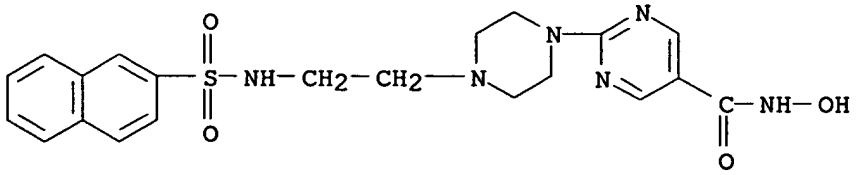


II

AB Title compds. I [Ar1 = (un)satd.-, (un)substituted-mono or fused poly-cyclic hydrocarbyl optionally contg. 1-4 heteroatoms per ring; R1 = (un)substituted-mono-, -bi-, -tri-cyclic-aryl or -heteroaryl; R2, R3, and R4 independently = H, halo, amino, etc.; R5 and R6 independently = H, alkyl, aryl, etc.; x = 0-1; Y = any pharmaceutically acceptable chem. moiety consisting of 1 to 50 atoms with provisions] and their pharmaceutically acceptable salts, are prepd. and disclosed as inhibitors of histone deacetylase. Thus, e.g., II was prepd. by Suzuki coupling of 2-bromo-2-nitro-phenylamine (prepn. given) with 2-thiopheneboronic acid followed by carbonylation with 4-[3,4-dimethoxy-(phenylamino)-methyl]benzoic acid (prepn. given) and subsequent redn. The inhibitory capability of I towards antiproliferative activity of histone deacetylase enzyme was evaluated using 3-[4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazolium] bromide (MTT) assay and it revealed that certain compds. of the invention had MTT IC 50 values in the range of below 1 up to 20 .mu.M. I as histone deacetylase inhibitors should prove useful in the treatment of diseases such as, but not limited to, cell proliferative disease, protozoal disease, and fungal disease.

IT **603954-02-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of amide derivs. as inhibitors of histone deacetylase)
RN 603954-02-5 CAPLUS
CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-[(2-naphthalenylsulfonyl)amino]ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

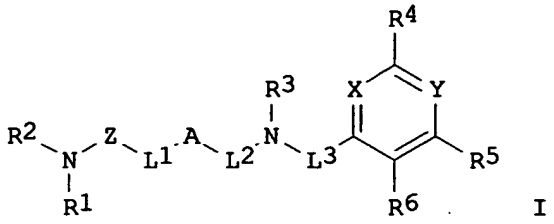


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

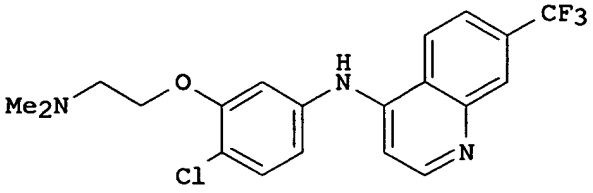
L8 ANSWER 5 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:220202 CAPLUS
DN 142:298126
TI Preparation of derivatives of pyridine, pyrimidine, quinoline, quinazoline, and naphthalene, useful as urotensin-II receptor antagonists
IN Wu, Chengde; Anderson, C. Eric; Bui, Huong; Dupre, Brian; Gao, Daxin; Holland, George W.; Kassir, Jamal; Li, Wen; Wang, Junmei
PA USA
SO U.S. Pat. Appl. Publ., 118 pp., Cont.-in-part of U.S. Ser. No. 783,916.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2005054850 | A1 | 20050310 | US 2004-924181 | 20040823 |
| | US 2004186102 | A1 | 20040923 | US 2004-783916 | 20040220 |
| PRAI | US 2003-451089P | P | 20030228 | | |
| | US 2004-783916 | A2 | 20040220 | | |

OS MARPAT 142:298126
GI



I



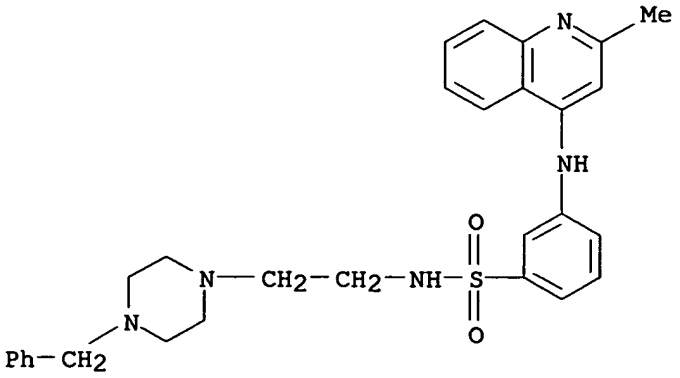
II

AB The invention relates to a prepn. of derivs. of pyridine, pyrimidine, quinoline, quinazoline, and naphthalene of formula I [wherein: A is (hetero)aryl, benzoheteroaryl, pyridone, pyridazinone, and pyrimidone; Z is (CH2)1-6; R1 and R2 are independently H, alkyl, or R1 and R2 along with N can form pyrrolidone or piperazine, etc.; R3 is H, alkyl, or arylalkyl; X and Y are independently C or N; R4, R5, and R6 are independently selected from H, alkyl, (hetero)aryl, halogen, or alkoxy, etc.; L1 is a single bond or O, C(O), SO2, or (hetero)arene; L2 and L3 are independently selected from a single bond, CH2, C(O), SO2, or NH], useful as urotensin-II receptor antagonists. Thus, e.g., II was prepd. by substitution of a 4-halo-7-trifluoromethylquinoline with 3-(2-dimethylaminoethoxy)-4-chloroaniline. The prepd. compds. were tested for inhibition of human [125I]-urotensin-II binding to urotensin-II receptor and inhibition of human urotensin-II-induced Ca2+ mobilization (for instance, for II IC50 was 6.5 .mu.M).

IT **758713-94-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of derivs. of pyridine, pyrimidine, quinoline, quinazoline, and naphthalene, useful as urotensin-II receptor antagonists)

RN 758713-94-9 CAPLUS

CN Benzenesulfonamide, 3-[(2-methyl-4-quinolinyl)amino]-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



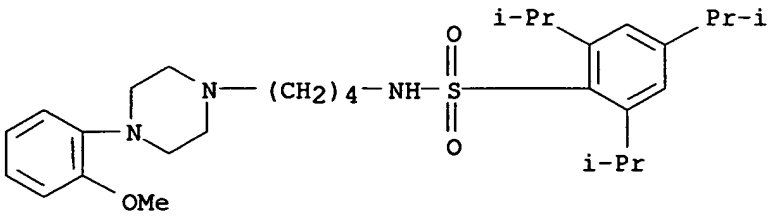
●2 HCl

L8 ANSWER 6 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:52602 CAPLUS
DN 143:305985
TI Pharmacomodulation of a sulfamide 5-HT6 receptor ligand
AU Renault, Jacques; Bernard, Aurelie; Brajeul, Solenn; Verhaeghe, Pierre; Butt, Sabrina; Fabis, Frederic; Dauphin, Francois; Uriac, Philippe; Rault, Sylvain
CS UPRES EA 2234- Institut de Chimie de Rennes, Faculte des Sciences Biologiques et Medicales, Universite de Rennes 1, Rennes, 35043, Fr.
SO Journal of Enzyme Inhibition and Medicinal Chemistry (2004), 19(6), 577-583
CODEN: JEIMAZ; ISSN: 1475-6366
PB Taylor & Francis Ltd.
DT Journal
LA English
AB A series of N-.omega.-aminoalkyl- or N-.omega.-amidinoalkyl-2,4,6-triisopropyl benzenesulfonamides has been synthesized and their resp. affinity indexes on 5-HT6 receptor detd. Amino-sulfonamide H2N(CH2)3NHSO2Ar (4; Ar = 2,4,6-triisopropylphenyl) was prepd. by polymer-assisted sulfonation of 3-aminopropylcarbamate; diamino-sulfonamides H2CH2(CH2)nCH2NHCH2(CH2)mCH2NHSO2Ar (7, m = 2, n = 1; 8,M = 1, n = 2) were prepd. by sulfonation of the corresponding bis-N-Boc-protected spermidine. Sulfonation of 4-amino-1-butanol afforded HO(CH2)4NHSO2Ar (9), its nosylation and treatment with piperidine gave N-(4-piperidinobutyl)-NHSO2Ar (12). Sulfonation of 4-(ZC6H4)-piperazine-1-butanamine gave ZC6H4N(CH2CH2)2N(CH2)4NHSO2Ar (19, 20; Z = 2-MeO, 4-F). Mercuridesulfuration of 1,3,4,5-tetrahydro-2H-1-benzazepine-2-thione in the presence of ArSO2NH(CH2)4NH2 (26) afforded cyclic amidine, N-[ArSO2NH(CH2)4]-3H-4,5-dihydrobenzazepine-2-amine (28). Compds. 4, 7-9, 12, 19, 20, 28 were tested for inhibition of [3H]LSD binding to human 5-HT6 receptors at 10-6 and 10-8 M concns. and compared to std. compd. 26 (JR435, Ki = 30 nM). This evaluation clearly showed that the compds. possessing an arylpiperazine moiety or an amidine function exhibited good affinity for the model.
IT **864941-50-4P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of aminoalkyl arenesulfonamides and sulfonylamido-alkyl amidines as human serotonin receptor pharmacomodulated ligands)

RN 864941-50-4 CAPLUS

CN Benzenesulfonamide, N-[4-[4-(2-methoxyphenyl)-1-piperazinyl]butyl]-2,4,6-tris(1-methylethyl)- (9CI) (CA INDEX NAME)




RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:1068075 CAPLUS

DN 142:168975

TI "Lead Hopping". Validation of Topomer Similarity as a Superior Predictor of Similar Biological Activities

AU Cramer, Richard D.; Jilek, Robert J.; Guessregen, Stefan; Clark, Stephanie J.; Wendt, Bernd; Clark, Robert D.

CS Tripos Discovery Research, Cornwall, EX23 8LY, UK

SO Journal of Medicinal Chemistry (2004), 47(27), 6777-6791
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

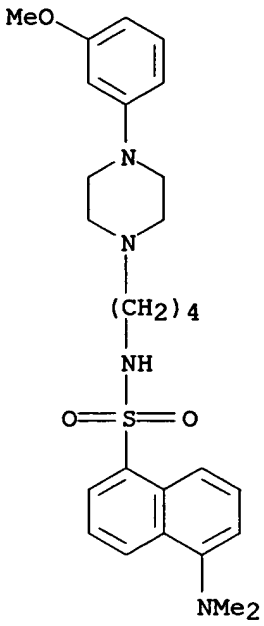
DT Journal

LA English

AB Two extensive studies quantifying the ability of topomer shape similarity to forecast a variety of biol. similarities are described. In a prospective trial of "lead hopping", using topomer similarity for virtual screening and queries from the patent literature, biol. assays of 308 selected compds. (representing 0.03% of those available, per assay type) yielded 11 successful "lead hops" in the 13 assays attempted. The hit rate averaged over all assays was 39% ("activity" defined as inhibition .gtoreq.20% at 10 .mu.M), significantly greater than an unexpectedly high neg. control hit rate of 15%. The av. "Tanimoto 2D fingerprint similarity" between query and "lead hop" structures (0.36) was little more than the Tanimoto similarity between random drug-like structures. Topomer shape and Tanimoto 2D fingerprint similarities were also compared retrospectively, in their tendencies to conc. together potential and actual drugs reported to belong to the same "activity class", for twenty classes. Among the most similar 3% of structures (corresponding to ".gtoreq.0.85 Tanimoto" for these structures), an av. of 62% of the topomer similar selection possessed a near neighbor belonging to the same activity class, roughly a one-third superiority over the "Tanimoto .gtoreq. 0.85" selection contg. 48% actives in avoiding false positives. Conversely, the least similar 75% of structures contained 0.3% actives for topomer similarity vs. 1.0% actives for Tanimoto 2D fingerprint similarity, a 3-fold superiority for topomers in avoiding false negatives.

IT **831238-74-5**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(validation of topomer similarity as a superior predictor of similar biol. activities of "Lead hopping")

RN 831238-74-5 CAPLUS
CN 1-Naphthalenesulfonamide, 5-(dimethylamino)-N-[4-[4-(3-methoxyphenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)




RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:916838 CAPLUS
DN 142:85846
TI Molecular docking and 3D QSAR studies on 1-amino-2-phenyl-4-(piperidin-1-yl)-butanes based on the structural modeling of human CCR5 receptor
AU Xu, Yong; Liu, Hong; Niu, Chunying; Luo, Cheng; Luo, Xiaomin; Shen, Jianhua; Chen, Kaixian; Jiang, Hualiang
CS Drug Discovery and Design Center, State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, 201203, Peop. Rep. China
SO Bioorganic & Medicinal Chemistry (2004), 12(23), 6193-6208
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
AB In the present study, we have used an approach combining protein structure modeling, mol. dynamics (MD) simulation, automated docking, and 3D QSAR analyses to investigate the detailed interactions of CCR5 with their antagonists. Homol. modeling and MD simulation were used to build the 3D model of CCR5 receptor based on the high-resoln. x-ray structure of bovine rhodopsin. A series of 64 CCR5 antagonists, 1-amino-2-phenyl-4-(piperidin-1-yl)-butanes, were docked into the putative binding site of the 3D model of CCR5 using the docking method, and the probable interaction model between CCR5 and the antagonists were obtained. The predicted binding affinities of the antagonists to CCR5 correlate well with the antagonist activities, and the interaction model could be used to explain many

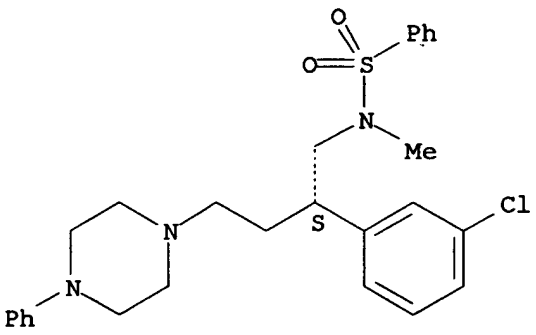
mutagenesis results. All these indicate that the 3D model of antagonist-CCR5 interaction is reliable. Based on the binding conformations and their alignment inside the binding pocket of CCR5, three-dimensional structure-activity relation (3D QSAR) analyses were performed on these antagonists using comparative mol. field anal. (CoMFA) and comparative mol. similarity anal. (CoMSIA) methods. Both CoMFA and CoMSIA provide statistically valid models with good correlation and predictive power. The q2(r2cross) values are 0.568 and 0.587 for CoMFA and CoMSIA, resp. The predictive ability of these models was validated by six compds. that were not included in the training set. Mapping these models back to the topol. of the active site of CCR5 leads to a better understanding of antagonist-CCR5 interaction. These results suggest that the 3D model of CCR5 can be used in structure-based drug design and the 3D QSAR models provide clear guidelines and accurate activity predictions for novel antagonist design.

IT **209160-71-4**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. docking and QSAR studies on piperidinylbutanes based on structural modeling of human CCR5 receptor)

RN 209160-71-4 CAPLUS

CN Benzenesulfonamide, N-[(2S)-2-(3-chlorophenyl)-4-(4-phenyl-1-piperazinyl)butyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:773121 CAPLUS

DN 141:424159

TI Novel 5-HT7 Receptor Inverse Agonists. Synthesis and Molecular Modeling of Arylpiperazine- and 1,2,3,4-Tetrahydroisoquinoline-Based Arylsulfonamides

AU Vermeulen, Erik S.; Van Smeden, Marjan; Schmidt, Anne W.; Sprouse, Jeffrey S.; Wikstroem, Haakan V.; Grol, Cor J.

CS Department of Medicinal Chemistry, Center for Pharmacy, State University of Groningen, Groningen, NL-9713, Neth.

SO Journal of Medicinal Chemistry (2004), 47(22), 5451-5466
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

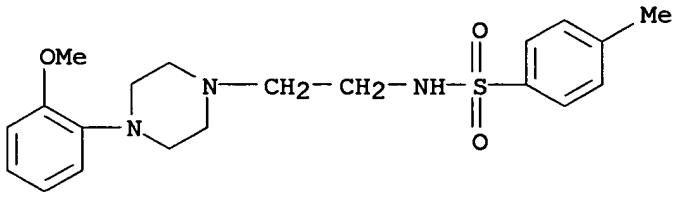
AB A series of arylpiperazine- and 1,2,3,4-tetrahydroisoquinoline-based

arylsulfonamides was synthesized and evaluated for their interactions with the constitutively active 5-HT7 receptor. Effects on basal adenylate cyclase activity were measured using HEK-293 cells expressing the rat 5-HT7. All ligands produced a decrease of adenylate cyclase activity, indicative of their inverse agonism. Addnl., computational studies with a set of 22 inverse agonists, including these novel inverse agonists and inverse agonists known from literature, resulted in a pharmacophore model and a CoMFA model (R2 = 0.97, SE = 0.18). Docking of inverse agonists at the binding site of a model of the helical parts of the 5-HT7 receptor, based on the .alpha. carbon template for 7-TM GPCRs, revealed interesting mol. interactions and a possible explanation for obsd. structure-activity relationships.

IT **793671-98-4P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and mol. modeling of arylpiperazinylalkyl- and 1,2,3,4-tetrahydroisoquinolinylalkylarylsulfonamides as 5-HT7 receptor inverse agonists)

RN 793671-98-4 CAPLUS

CN Benzenesulfonamide, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-methyl- (9CI) (CA INDEX NAME)



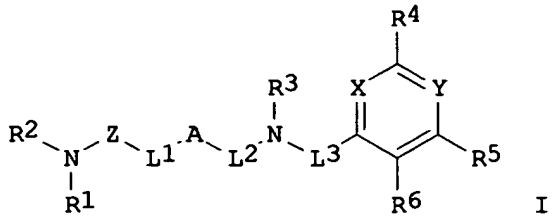

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:754408 CAPLUS
DN 141:277630
TI A preparation of derivatives of pyridine, pyrimidine, quinoline, quinazoline, and naphthalene, useful as urotensin-II receptor antagonists
IN Wu, Chengde; Anderson, C. Eric; Bui, Huong; Gao, Daxin; Holland, George W.; Kassir, Jamal; Li, Wen; Wang, Junmei; Dupre, Brian
PA Encysive Pharmaceuticals Inc., USA
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

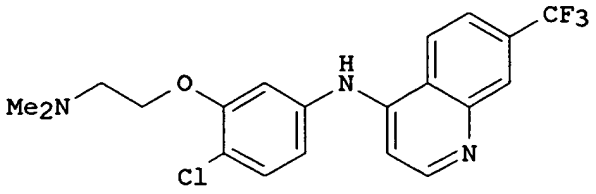
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004078114 | A2 | 20040916 | WO 2004-US5150 | 20040220 |
| | WO 2004078114 | A3 | 20050217 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,

MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2517166 AA 20040916 CA 2004-2517166 20040220
EP 1603884 A2 20051214 EP 2004-713383 20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI US 2003-451089P P 20030228
WO 2004-US5150 W 20040220
OS MARPAT 141:277630
GI



I



II

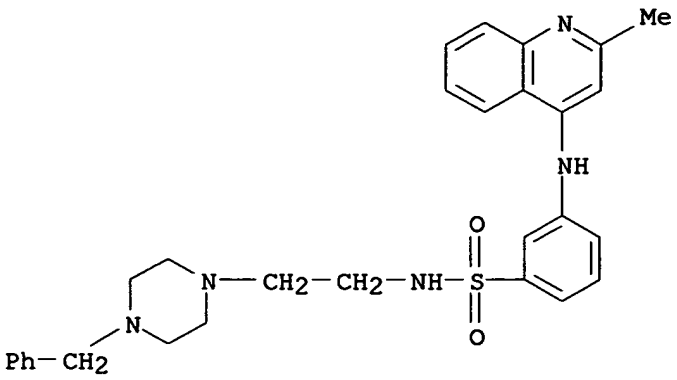
AB The invention relates to a prepn. of derivs. of pyridine, pyrimidine, quinoline, quinazoline, and naphthalene of formula I [wherein: A is (hetero)aryl, benzoheteroaryl, pyridone, pyridazinone, and pyrimidone; Z is (CH2)1-6; R1 and R2 are independently H, alkyl, or R1 and R2 along with N can form pyrrolidone or piperazine, etc.; R3 is H, alkyl, or arylalkyl; X and Y are independently C or N; R4, R5, and R6 are independently selected from H, alkyl, (hetero)aryl, halogen, or alkoxy, etc.; L1 is a single bond or O, C(O), SO2, or (hetero)arene; L2 and L3 are independently selected from a single bond, CH2, C(O), SO2, or NH], useful as urotensin-II receptor antagonists. The prepd. compds. were tested for inhibition of human [125I]-urotensin-II binding to urotensin-II receptor and inhibition of human urotensin-II-induced Ca2+ mobilization (for instance, for II IC50 was 6.5 .mu.M).

IT **758713-94-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of derivs. of pyridine, pyrimidine, quinoline, quinazoline, and naphthalene, useful as urotensin-II receptor antagonists)

RN 758713-94-9 CAPLUS

CN Benzenesulfonamide, 3-[(2-methyl-4-quinolinyl)amino]-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX

NAME)

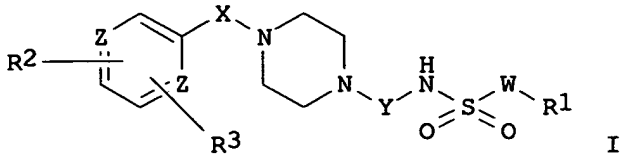


●2 HCl

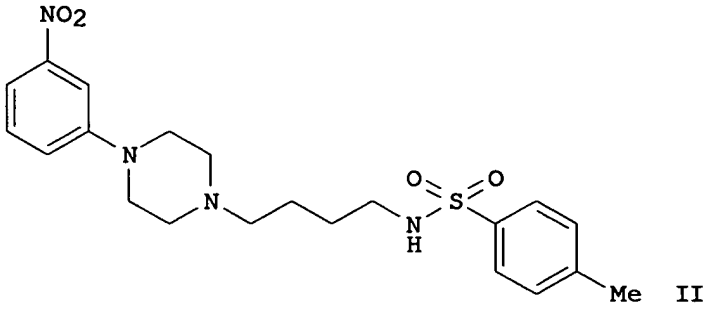
L8 ANSWER 11 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:675719 CAPLUS
DN 141:207226
TI Preparation of arylpiperazinyl sulfonamides as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating CND disorders, especially anxiety and related diseases
IN Dhanoa, Dale S.; Chen, Dongli; Becker, Oren; Noiman, Silvia; Cheruku, Srinivasa Rao; Marantz, Yael; Sharadendu, Anurag; Shachem, Sharon; Heifetz, Alexander; Mohanty, Pradyumna; Inbal, Boaz; Fichman, Merav; Nudelman, Raphael; Bar-Haim, Shay
PA Predix Pharmaceuticals Holdings, Inc., USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004069794 | A2 | 20040819 | WO 2004-US2858 | 20040202 |
| | WO 2004069794 | A3 | 20041104 | | |
| | WO 2004069794 | C2 | 20041209 | | |
| | WO 2004069794 | B1 | 20050127 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2004220192 | A1 | 20041104 | US 2004-768579 | 20040130 |
| | CA 2513915 | AA | 20040819 | CA 2004-2513915 | 20040202 |
| | EP 1592425 | A2 | 20051109 | EP 2004-707409 | 20040202 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRAI US 2003-443988P P 20030131
US 2003-458297P P 20030328
US 2003-503520P P 20030916
US 2004-768579 A2 20040130
WO 2004-US2858 W 20040202
OS MARPAT 141:207226
GI



I



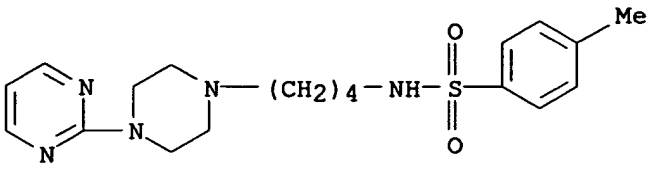
II

AB Title compds. I [wherein R1 = (un)substituted alkyl-aryl, cyclo/alkyl; R2, R3 = independently H, lower alkyl, cycloalkyl, trihalomethyl, halo, etc.; Z = N or C; X = (CH2)m; m = 0-6; Y = (CH2)n; n = 1-6; W = (CH2)p; p = 0-4; N together with one or several carbons from Y = 4-, 5-, 6- or 7-membered hetero/cyclic ring; their pharmaceutically acceptable salts and/or esters, and provided that when p=o, R1 is not (un)substituted aryl and R2, R3 are independently other than alkoxy/phenyl] were prepd. as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating anxiety and related disorders. Three biol. examples are given. For example, II.bul.2HCl was prepd., in 3 steps, from 1-amino-4-butanol, tosyl chloride, 1-(3-nitrophenyl)piperazine, and HCl. Selected I bound to 5-HT1A receptor with Ki values in the 1.3 - 26 nM range. Thus, I are useful for treating central nervous system disorders such as generalized anxiety disorder, ADD/ADHD, neural injury, stroke, and migraine.

IT **690949-14-5P**, 4-Methyl-N-[4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl]benzenesulfonamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(5-HT1 agonist; prepn. of arylpiperazinyl sulfonamides as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating anxiety and related disorders)

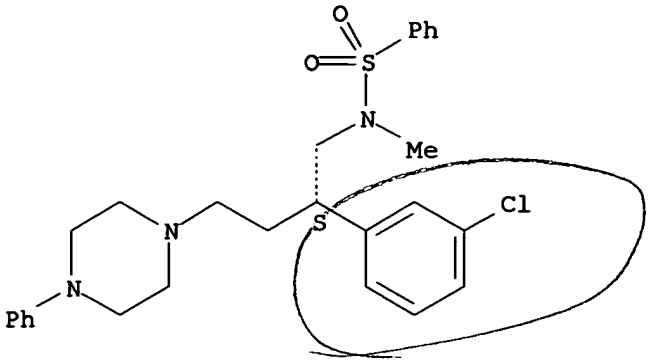
RN 690949-14-5 CAPLUS

CN Benzenesulfonamide, 4-methyl-N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 12 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:34787 CAPLUS
DN 140:385496
TI Three-dimensional quantitative structure-activity relationship analyses of piperidine-based CCR5 receptor antagonists
AU Song, Minghu; Breneman, Curt M.; Sukumar, N.
CS Department of Chemistry, Rensselaer Polytechnic Institute, Troy, NY, 12180, USA
SO Bioorganic & Medicinal Chemistry (2004), 12(2), 489-499
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Ltd.
DT Journal
LA English
AB The CCR5 chemokine receptor has recently been found to play a crucial role in the viral entry stage of HIV infection and has therefore become an attractive potential target for anti-HIV therapeutics. The lack of CCR5 crystal structure data has impeded the development of structure-based CCR5 antagonist design. In this paper, we compare two three-dimensional Quant. Structure-Activity Relationship (3D-QSAR) methods: Comparative Mol. Field Anal. (CoMFA) and Comparative Mol. Similarity Indexes Anal. (CoMSIA) on a series of piperidine-based CCR5 antagonists as an alternative approach to investigate the interaction between CCR5 antagonists and their receptor. Superimposition of antagonist structures was performed using two alignment rules: at./centroid rms fit and rigid body field fit techniques. The 3D QSAR models were derived from a training set of 72 compds., and were found to have predictive capability for a set of 19 holdout test compds. The resulting contour maps produced by the best CoMFA and CoMSIA models were used to identify the structural features relevant to biol. activity in this series of compds. Further analyses of these interaction-field contour maps also showed a high level of internal consistency.
IT **209160-71-4**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(QSAR CoMFA and CoMSIA analyses of piperidine-based CCR5 receptor antagonists)
RN 209160-71-4 CAPLUS
CN Benzenesulfonamide, N-[(2S)-2-(3-chlorophenyl)-4-(4-phenyl-1-piperazinyl)butyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

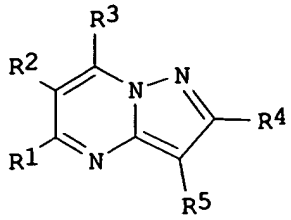



RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:875291 CAPLUS
DN 139:350751
TI Preparation of pyrazolo[1,5-a]pyrimidine derivatives as NAD(P)H oxidase inhibitors
IN Seno, Kaoru; Nishi, Koichi; Matsuo, Yoshiyuki; Fujishita, Toshio
PA Shionogi & Co., Ltd., Japan
SO PCT Int. Appl., 240 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003091256 | A1 | 20031106 | WO 2003-JP5024 | 20030418 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2483306 | AA | 20031106 | CA 2003-2483306 | 20030418 |
| | EP 1505068 | A1 | 20050209 | EP 2003-717663 | 20030418 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | BR 2003009475 | A | 20050301 | BR 2003-9475 | 20030418 |
| PRAI | JP 2002-121519 | A | 20020423 | | |
| | WO 2003-JP5024 | W | 20030418 | | |

OS MARPAT 139:350751
GI



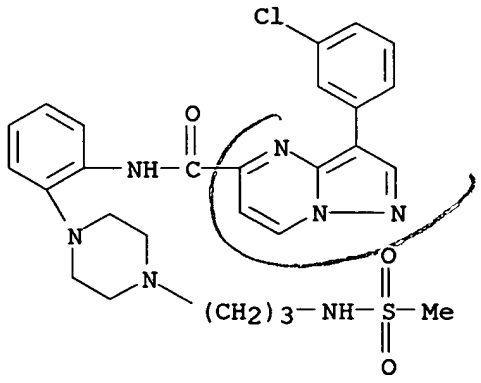
I

AB Title compds. I (R1, R2, R3, R4, R5 = H, halo, alkyl, alkenyl, alkynyl, cycloalkyl, , aryl, heteroaryl, etc.) and their pharmaceutically acceptable salts, useful in the prevention of or treatments for diseases relating to NAD(P)H, are prepd. Thus, N-2-cyclohexylphenyl 3-(3-chlorophenyl)pyrazolo[1,5-a]pyrimidin-5-amide was prepd. in several steps from Et 7-chloropyrazolo[1,5-a]pyrimidine-5-carboxylate.

IT **619304-62-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazolo[1,5-a]pyrimidine derivs. as NAD(P)H oxidase inhibitors)

RN 619304-62-0 CAPLUS

CN Pyrazolo[1,5-a]pyrimidine-5-carboxamide, 3-(3-chlorophenyl)-N-[2-[4-[3-[(methylsulfonyl)amino]propyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 109 THERE ARE 109 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:796691 CAPLUS

DN 139:307788

TI Preparation of 5-cyanopyrimidine derivatives as anti-inflammatory agents

IN Machii, Daisuke; Yamaura, Yosuke; Arai, Hitoshi; Yanagawa, Koji; Ohshima, Etsuo; Kawanabe, Ari; Iwase, Miho; Kobayashi, Katsuya; Sato, Takashi; Miki, Ichiro

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO PCT Int. Appl., 169 pp.
CODEN: PIXXD2

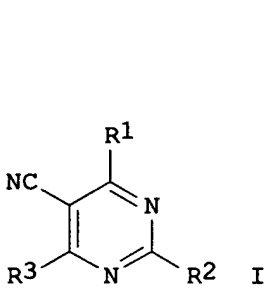
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003082855 | A1 | 20031009 | WO 2003-JP4009 | 20030328 |

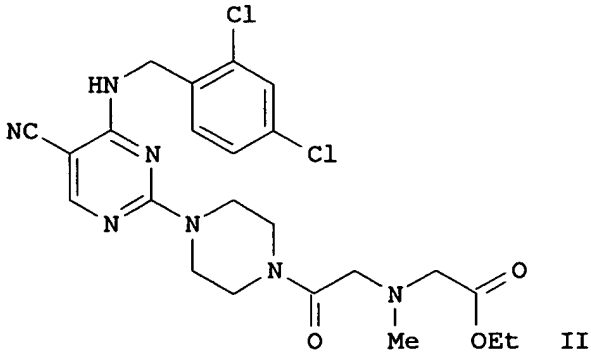
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI JP 2002-90640 A 20020328
OS MARPAT 139:307788
GI




I

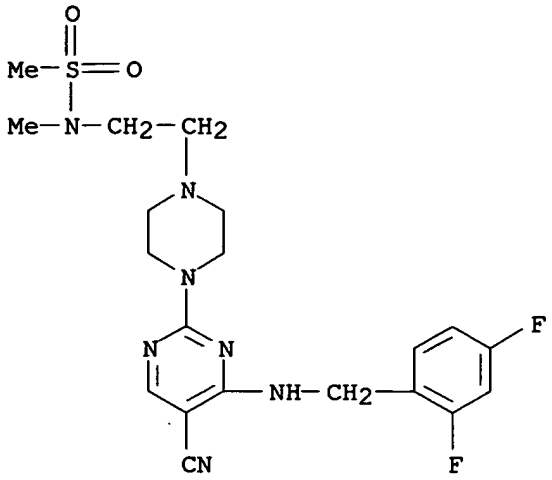



II

AB The title pyrimidine compds. I [wherein R1 and R3 = independently H, OH, halo, (un)substituted alkyl, alkoxy, alkylthio, aryl, aralkyl, or amino; R2 = (un)substituted amino] or ammonium salts or pharmaceutically acceptable salts thereof are prepd. as anti-inflammatory agents. For example, the compd. II was prepd. in a multi-step synthesis. II showed 97% inhibitory activity against thymus and activation-regulated chemokine (TARC) Hut78 cells at 1 .mu.M. Formulations contg. I as an active ingredient were also described.

IT **611203-73-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of cyanopyrimidine derivs. as anti-inflammatory agents)

RN 611203-73-7 CAPLUS
CN Methanesulfonamide, N-[2-[4-[5-cyano-4-[[(2,4-difluorophenyl)methyl]amino]-2-pyrimidinyl]-1-piperazinyl]ethyl]-N-methyl- (9CI) (CA INDEX NAME)

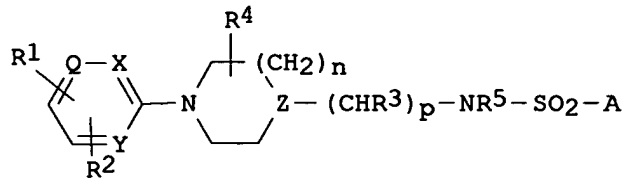


RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

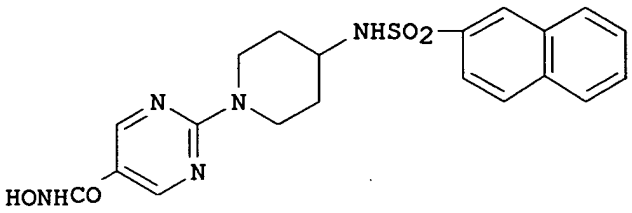
L8 ANSWER 15 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:737724 CAPLUS
DN 139:276820
TI Preparation of sulfonylaminopiperidine derivatives as inhibitors of histone deacetylase
IN Van Emelen, Kristof; Backx, Leo Jacobus Jozef; Van Brandt, Sven Franciscus Anna; Angibaud, Patrick Rene; Pilatte, Isabelle Noeelle Constance; Verdonck, Marc Gustaaf Celine; De Winter, Hans Louis Jos
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 8

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003076401 | A1 | 20030918 | WO 2003-EP2517 | 20030311 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2476186 | AA | 20030918 | CA 2003-2476186 | 20030311 |
| | EP 1485354 | A1 | 20041215 | EP 2003-743874 | 20030311 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | BR 2003007599 | A | 20050201 | BR 2003-7599 | 20030311 |
| | US 2005171347 | A1 | 20050804 | US 2003-507159 | 20030311 |
| | JP 2005526763 | T2 | 20050908 | JP 2003-574622 | 20030311 |
| | NO 2004004224 | A | 20041005 | NO 2004-4224 | 20041005 |

PRAI US 2002-363799P P 20020313
WO 2002-EP14481 A 20021218
WO 2002-EP14081 A 20021218
WO 2003-EP2517 W 20030311
OS MARPAT 139:276820
GI



I



II

AB The title compds. I [Q, X, Y, Z = N, (un)substituted CH; R1 = (un)substituted CONH2, NHCHO, COalkanediylSH, CONHOH, NHCOC:NHOH or other Zn-chelating group; R2 = H, halogen, OH, amino, NO2, alkyl, alkoxy, CF3, dialkylamino, NHOH, naphthalenylsulfonylpyrazinyl; R3 = H, aryl; R4 = H, OH, amino, (un)substituted alkyl, alkoxy, CONH2, CO2H; R5 = H, alkyl, cycloalkyl, hydroxyalkyl, alkoxyalkyl, dialkylaminoalkyl, aryl; A = (un)substituted Ph, cyclohexyl, heterocyclic, heteroaryl, naphthyl; n = 0-3; p = 0-4] were prepd. for use as histone deacetylase inhibitors in the treatment of proliferative diseases. Thus, the sulfonylaminopiperidine II was prepd. from Et 4-aminopiperidine-1-carboxylate, 2-naphthalenesulfonyl chloride, and Et 2-methylsulfonylpyrimidine-5-carboxylate in 6 steps. II had pIC50 for inhibition of histone deacetylase of 6.523 and for antiproliferative activity against A2780 cells of 5.277.

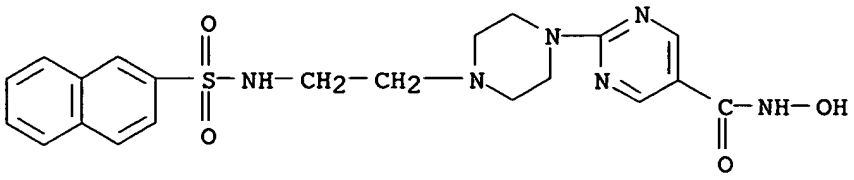
IT **603954-03-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonylaminopiperidine derivs. as inhibitors of histone deacetylase)

RN 603954-03-6 CAPLUS

CN 5-Pyrimidinecarboxamide, N-hydroxy-2-[4-[2-[(2-naphthalenylsulfonyl)amino]ethyl]-1-piperazinyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

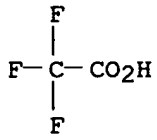
CM 1

CRN 603954-02-5
CMF C21 H24 N6 O4 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2

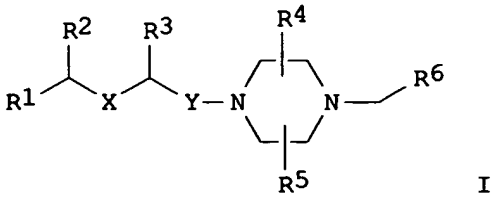


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

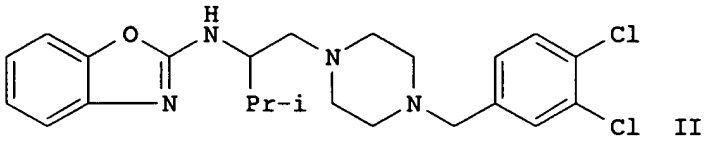
L8 ANSWER 16 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:656757 CAPLUS
DN 139:197507
TI Preparation of piperazine derivatives as anti-inflammatory agents
IN Dowle, Michael Dennis; Eldred, Colin David; Johnson, Martin Redpath; Redfern, Tracy Jane; Robinson, John Edward; Trivedi, Naimisha; Weller, Victoria
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003068759 | A1 | 20030821 | WO 2003-GB583 | 20030210 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1480959 | A1 | 20041201 | EP 2003-739556 | 20030210 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | JP 2005528342 | T2 | 20050922 | JP 2003-567889 | 20030210 |
| PRAI | GB 2002-3299 | A | 20020212 | | |
| | WO 2003-GB583 | W | 20030210 | | |

OS MARPAT 139:197507
GI



I



II

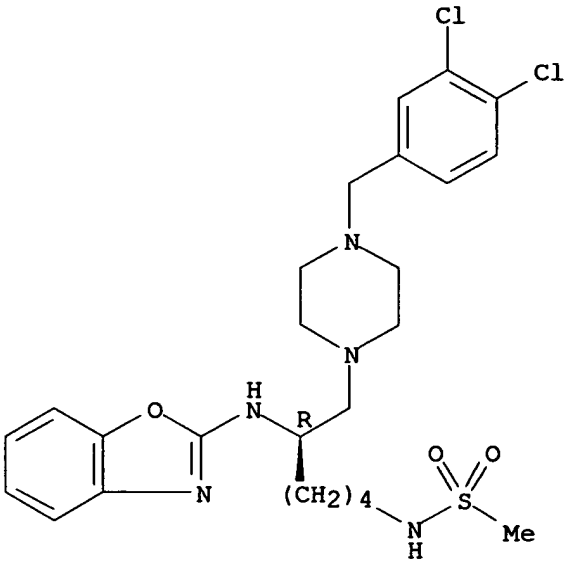
AB Title compds. I [R1 = (un)substituted (hetero)aryl; R2 = H, alkyl, alkenyl, cycloalkyl; X, Y = bond or (CH2)1-2 where X and Y do not both represent a bond; R3 = alkyl, alkenyl, (hetero)aryl, etc.; R4-5 = H, alkyl, carboxy, etc.; R6 = (hetero)aryl] are prepd. For instance, 4-[(3,4-dichlorophenyl)methyl]-.alpha.-(1-methylethyl)-1-piperazineethaneamine is reacted with 2-chlorobenzoxazole (i-PrOH, i-Pr2NEt, reflux, 18 h),to give II. Compds. of the invention have functional pKi values in the range of 5.5-7.5 in the CCR-3 eosinophil chemotaxis assay. I are useful as anti-inflammatory agents.

IT **583868-41-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazine CCR-3 antagonists useful as anti-inflammatory agents)

RN 583868-41-1 CAPLUS

CN Methanesulfonamide, N-[(5R)-5-(2-benzoxazolylamino)-6-[4-[(3,4-dichlorophenyl)methyl]-1-piperazinyl]hexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

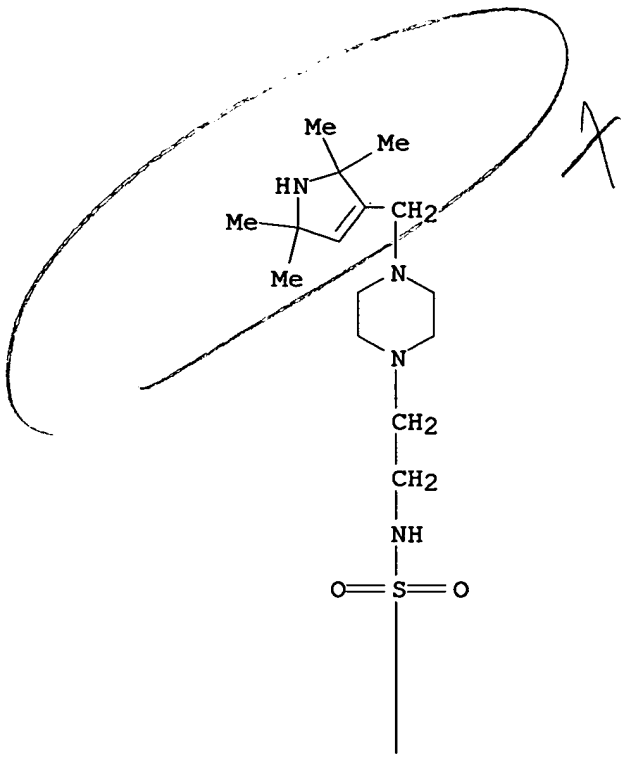
L8 ANSWER 17 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:91523 CAPLUS
DN 139:303965
TI Interaction of singlet molecular oxygen with double fluorescent and spin sensors
AU Bilski, P.; Hideg, K.; Kalai, T.; Bilska, M. A.; Chignell, C. F.
CS Laboratory of Pharmacology and Chemistry, NIEHS/NIH, Research Triangle Park, NC, USA
SO Free Radical Biology & Medicine (2003), 34(4), 489-495
CODEN: FRBMEH; ISSN: 0891-5849
PB Elsevier Science Inc.
DT Journal
LA English
AB Double fluorescent and spin sensors were recently used to detect transient oxidants via simultaneous fluorescence change and prodn. of the nitroxide radical detected by ESR. One such oxidant, singlet mol. oxygen (1O2), was detected in thylakoid membrane using these probes. In the present study, we investigated the total (phys. and chem.) quenching of 1O2 phosphorescence by sensors composed of the 2,5-dihydro-2,2,5,5-tetramethyl-1H-pyrrole moiety attached to xanthene or dansyl fluorophores. We found that the quenching rate consts. were in the range (2-7) .times. 107 M-1s-1 in acetonitrile and D2O. Quenching of 1O2 is usually an additive process in which different functional groups may contribute. We estd. that the 1O2 quenching by the amine fragments was ca. one to two orders of magnitude lower than that for the complete mols. Our data suggest that the incorporation of a fluorescent chromophore results in addnl. strong quenching of 1O2, which may in turn decrease the nitroxide yield via the 1O2 chem. path, possibly having an effect on quant. interpretations. We have also found that probes with the dansyl fluorophore photosensitized 1O2 upon UV excitation with the quantum yield of 0.087 in acetonitrile at 366 nm. This result shows that care must be taken when the dansyl-based sensors are used in expts. requiring UV irradn. We hope that our results

will contribute to a better characterization and wider use of these novel double sensors.

IT **505074-73-7**, HO 2780
RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process); USES (Uses)
(kinetics of phosphorescence quenching of singlet mol. oxygen by double fluorescent and spin sensors)

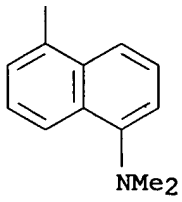
RN 505074-73-7 CAPLUS

CN 1-Naphthalenesulfonamide, N-[2-[4-[(2,5-dihydro-2,2,5,5-tetramethyl-1H-pyrrol-3-yl)methyl]-1-piperazinyl]ethyl]-5-(dimethylamino)- (9CI) (CA INDEX NAME)




PAGE 1-A

PAGE 2-A

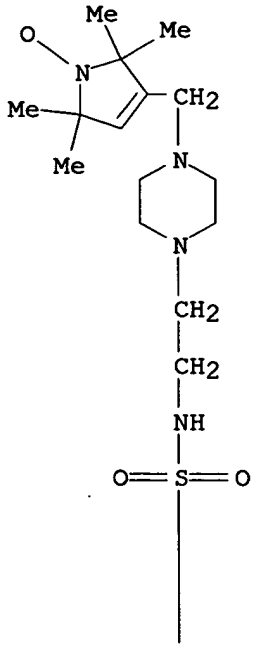



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

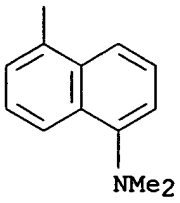
L8 ANSWER 18 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:718019 CAPLUS

DN 138:287634
TI Synthesis and structure optimization of double (fluorescent and spin) sensor molecules
AU Kalai, Tamas; Hankovszky, Olga H.; Hideg, Eva; Jeko, Jozsef; Hideg, Kalman
CS Institute of Organic and Medicinal Chemistry, University of Pecs, Pecs, H-7643, Hung.
SO ARKIVOC (Gainesville, FL, United States) [online computer file] (2002), (3), 112-120
CODEN: AGFUAR
URL: http://www.arkat-usa.org/ark/journal/2002/Lloyd/DL-297G/DL-297G.pdf
PB Arkat USA Inc.
DT Journal; (online computer file)
LA English
OS CASREACT 138:287634
AB Synthesis and fluorescence properties of stable nitroxide free radicals (101, 11a, 12a, 14a, 20a, 21a) and their amine (10b, 11b, 12b, 14b, 20b, 21b) precursors covalently linked to dansyl or 3- and 4-aminophthalimide are reported. The best intramol. quenching is achieved when the fluorophore and the nitroxide are in the closest possible position.
IT **505074-72-6P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and fluorescence of nitroxide free radicals for fluorescent and spin sensor mols.)
RN 505074-72-6 CAPLUS
CN 1H-Pyrrol-1-yloxy, 3-[[4-[2-[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]amino]ethyl]-1-piperazinyl]methyl]-2,5-dihydro-2,2,5,5-tetramethyl- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

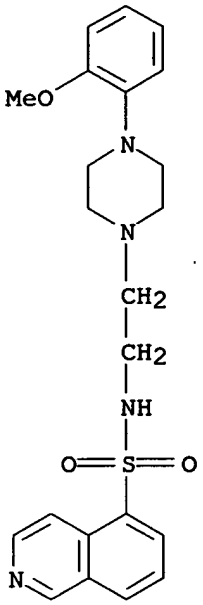



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:444494 CAPLUS
DN 137:28321
TI Use of certain isoquinolinesulfonyl compounds for the treatment of glaucoma and ocular ischemia
IN Hellberg, Mark R.; Kapin, Michael A.; Desantis, Louis M., Jr.
PA Alcon Laboratories, Inc., USA
SO U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 77,575.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 6403590 | B1 | 20020611 | US 2001-919301 | 20010731 |
| | WO 9723222 | A1 | 19970703 | WO 1996-US20197 | 19961220 |
| | W: AU, CA, CN, JP, KR, MX, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | US 6271224 | B1 | 20010807 | US 1999-77575 | 19990119 |
| PRAI | US 1995-9351P | P | 19951221 | | |
| | WO 1996-US20197 | W | 19961220 | | |
| | US 1999-77575 | A2 | 19990119 | | |

OS MARPAT 137:28321
AB Isoquinolinesulfonyl compds. are used in ophthalmic compns. to treat glaucoma or other ischemic-borne ocular disorders, e.g. retinopathies or optic neuropathies. These compds. vasodilate ocular blood vessels, lower IOP and prevent or reduce the progression of visual field loss. Prepn. and testing of 1-(5-isoquinolinesulfonyl)-2,5-dimethylpiperazine are described.
IT **192712-45-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isoquinolinesulfonyl compds. for treatment of glaucoma and ocular ischemia)
RN 192712-45-1 CAPLUS
CN 5-Isoquinolinesulfonamide, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-(9CI) (CA INDEX NAME)



RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

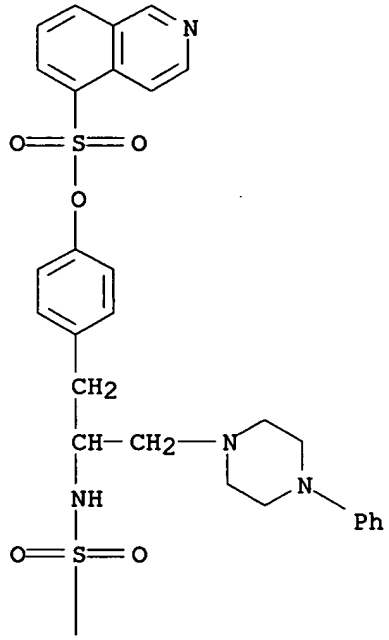
L8 ANSWER 20 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:325400 CAPLUS
DN 137:73653
TI Characteristics of ATP-induced current through P2X7 receptor in NG108-15 cells: unique antagonist sensitivity and lack of pore formation
AU Watano, Tomokazu; Matsuoka, Isao; Kimura, Junko
CS Department of Pharmacology, Fukushima Medical University School of Medicine, Fukushima, 960-1295, Japan
SO Japanese Journal of Pharmacology (2002), 88(4), 428-435
CODEN: JJPAAZ; ISSN: 0021-5198
PB Japanese Pharmacological Society
DT Journal
LA English
AB ATP activates the mouse P2X7 receptor and induces a nonselective-cation current in NG108-15 cells. We investigated the effects of five receptor antagonists on the ATP-induced nonselective-cation current through P2X7 receptor (INS.cntdot.P2X7) in NG108-15 cells. Nonselective P2 receptor antagonists, RB-2, PPADS and suramin inhibited the INS.cntdot.P2X7 with IC50 values of 4.3, 53 and 40 .mu.M, resp. However, KN-04, which is a potent antagonist of human P2X7 receptors but is not that of rat P2X7 receptors, had only a weak blocking effect. Furthermore, oxidized-ATP (300 .mu.M), an antagonist of the P2X7 receptor-mediated pore-formation, did not affect the INS.cntdot.P2X7. Prolonged ATP application did not increase the membrane permeability to large mols., N-methyl-D-glucamine or Yo-Pro-1, indicating that pore-formation was not promoted by the P2X7 receptor activation in NG108-15 cells. These results suggest that antagonist sensitivities and pore-forming properties of the P2X7 receptors in NG108-15 cells are different from those of other cells types.
IT **129695-80-3**, KN-04
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(ATP-induced current through P2X7 receptor in NG108-15 cells with unique antagonist sensitivity and lack of pore formation)

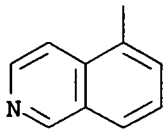
RN 129695-80-3 CAPLUS

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:314395 CAPLUS

DN 136:335540

TI Use of PDE V inhibitors for improved fecundity in mammals

IN Westbrook, Simon Lempriere; Zanzinger, Johannes Friedrich

PA Pfizer Limited, UK; Pfizer Inc.

SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

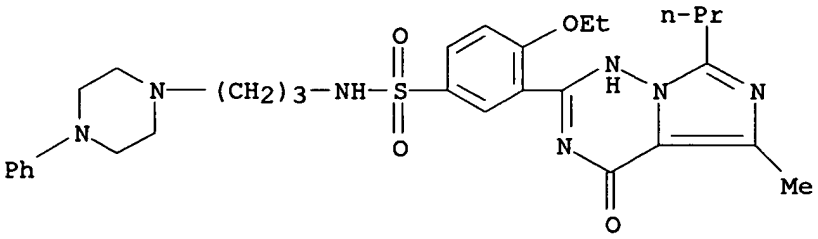
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 1199070 | A2 | 20020424 | EP 2001-308684 | 20011011 |
| | EP 1199070 | A3 | 20040317 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | CA 2359383 | AA | 20020420 | CA 2001-2359383 | 20011018 |
| | US 2003018036 | A1 | 20030123 | US 2001-982445 | 20011018 |
| | US 6548508 | B2 | 20030415 | | |
| | AU 2001081523 | A5 | 20020502 | AU 2001-81523 | 20011019 |
| | JP 2002220346 | A2 | 20020809 | JP 2001-322195 | 20011019 |
| | ZA 2001008617 | A | 20030422 | ZA 2001-8617 | 20011019 |
| | NZ 514947 | A | 20050324 | NZ 2001-514947 | 20011019 |
| | US 2003018037 | A1 | 20030123 | US 2002-229534 | 20020827 |
| | US 6743799 | B2 | 20040601 | | |
| | US 2004167095 | A1 | 20040826 | US 2004-778866 | 20040212 |
| PRAI | GB 2000-25782 | A | 20001020 | | |
| | US 2000-253338P | P | 20001128 | | |
| | US 2001-982445 | A1 | 20011018 | | |
| | US 2002-229534 | A1 | 20020827 | | |

AB The invention relates to the use of a cyclic guanosine 3',5'-monophosphate phosphodiesterase type five (cGMP PDE V) inhibitor for increasing fecundity in a mammal by one or more of (a) promoting the growth of an oocyte, zygote, blastocyst, embryo and/or fetus, (b) increasing the rate or probability of survival of an embryo and/or fetus and (c) increasing the birth wt. of a progeny, or for increasing milk productivity. I.v. and tablet formulations are exemplified. Formulations and packs contg. the PDE V inhibitors for pharmaceutical or veterinary use are claimed.

IT **224787-56-8**
RL: AGR (Agricultural use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of PDE V inhibitors for improved fecundity in mammals)

RN 224787-56-8 CAPLUS

CN Benzenesulfonamide, 3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxy-N-[3-(4-phenyl-1-piperazinyl)propyl]-(9CI) (CA INDEX NAME)




L8 ANSWER 22 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:161742 CAPLUS
DN 136:291079
TI New derivatives of the 5-HT1A antagonist WAY 100635
AU Hocke, Carsten
CS Germany
SO Berichte des Forschungszentrums Juelich (2001), Juel-3895, i-viii, 1-133
CODEN: FJBEE5; ISSN: 0366-0885
DT Report

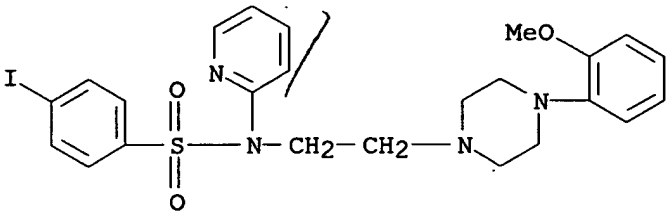
LA German

AB The serotonergic system with its different receptor subtypes is one of the most important neuronal transmitter systems in the brain. It is involved in the regulation of various physiol. functions and states of mind such as fear, depression and schizophrenia. The radioligand [11C]WAY-100635 ([11C]N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-(2-pyridinyl)-cyclohexanecarboxamide) was successfully used in vivo as 5-HT1A antagonist. The aim of the study was to prep. in vivo stable 18F-analogs. New derivatization of WAY 100635 was at first performed by n.c.a. 18F-labeling in 4-position of the cyclohexyl group in a one-step reaction. With the diastereomeric model compds. cis/trans ethyl-4-tosylcyclohexanecarboxylate the dependence of various reaction parameters, like temp., solvent and reaction time, on the radiochem. yield (RCY) was tested. The results were transferred to the WAY derivs. The best results of n.c.a. 18F-fluorination were obtained at 100.degree.C using DMSO as solvent. The radiochem. yield was about 25% for the cis-diastereomer and 5% for the trans-diastereomer of 4-[18F]fluoro-(N-2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-N-(2-pyridinyl)-cyclohexanecarboxamide. Subsequently, the syntheses of stabilized sulfonamides and sulfinamides as new analogs of the 5-HT1A antagonist WAY 100635 were performed. The derivs. were radiolabeled with [18F]fluoride and [123I]iodide for in vivo applications; namely 4-iodo- and 4-fluoro-N-{2-(4-(2-methoxyphenyl)-piperazine-1-yl)-ethyl}-N-pyridin-2-yl-benzenesulfonamide as well as the corresponding sulfinamide analogs. With the activating sulfonamide substituent different leaving groups (X = F, Cl, Br, I and NO2) were investigated for no-carrier-added arom. 18F-substitution. Again the effect of various reaction parameters, like temp., solvent and leaving groups, on the max. radiochem. yield was tested in model compds. The results were transfered to the compds. of interest. The 18F-labeled sulfonamides were prepd. by nucleophilic arom. substitution in high RCY of 65% within 15 min using bromine as leaving group at 160.degree.C and DMSO as solvent. The corresponding 18F-labeled sulfinamides were not stable under the labeling conditions tested. The formation of [123I]iodo-analogs of sulfonamides was accomplished by Cu(I)-assisted radioiodo-for-bromo substitution in acetic acid with over 90% RCY. Finally, the 123I-labeled sulfinamide was prepd. via electrophilic destannylation. The RCY of 4-[123I]iodo-N-{2-[4-(2-methoxyphenyl)-piperazin- 1-yl]-ethyl}-N-pyridin-2-yl-benzenesulfinamide was ca. 80% after 2 min in methanol/acetic acid at ambient temp. with chloramine-T as in-situ oxidizing agent. In vitro competition studies with the fluoro- and iodo-sulfonamides and -sulfinamides vs. the highly selective 5-HT1A receptor ligand [3H]8-OH-DPAT lead to Ki values of 36 to 112 nM. First biodistribution studies in mice of [18F]fluoro-sulfonamide proved the increased in vivo stability.

IT **407636-07-1DP**, radiolabeled
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(5-HT1A receptor antagonist WAY 100635 derivs. for PET and SPET)

RN 407636-07-1 CAPLUS

CN Benzenesulfonamide, 4-iodo-N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-2-pyridinyl- (9CI) (CA INDEX NAME)




RE.CNT 208 THERE ARE 208 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:142707 CAPLUS
DN 136:200181
TI Substituted and/or fused pyrazoles, particularly piperazinylpropyl-substituted pyrazolopyridines, useful as cathepsin S inhibitors, and their pharmaceutical compositions and use as immunosuppressants
IN Breitenbucher, J. Guy; Cai, Hui; Edwards, James P.; Grice, Cheryl A.; Gustin, Darin J.; Khatuya, Haripada; Meduna, Steven P.; Pio, Barbara A.; Tays, Kevin L.; Wei, Jianmei
PA Ortho McNeil Pharmaceutical, Inc., USA
SO PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 8

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2002014314 | A2 | 20020221 | WO 2001-US25289 | 20010810 |
| | WO 2002014314 | A3 | 20020606 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2419540 | AA | 20020221 | CA 2001-2419540 | 20010810 |
| | AU 2001081255 | A5 | 20020225 | AU 2001-81255 | 20010810 |
| | US 2002040020 | A1 | 20020404 | US 2001-928122 | 20010810 |
| | EP 1309591 | A2 | 20030514 | EP 2001-959731 | 20010810 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | JP 2004512272 | T2 | 20040422 | JP 2002-519454 | 20010810 |
| | NZ 524193 | A | 20041224 | NZ 2001-524193 | 20010810 |
| | ZA 2003002052 | A | 20040623 | ZA 2003-2052 | 20030313 |
| PRAI | US 2000-225138P | P | 20000814 | | |
| | US 2001-928122 | A | 20010810 | | |
| | WO 2001-US25289 | W | 20010810 | | |

OS MARPAT 136:200181
GI

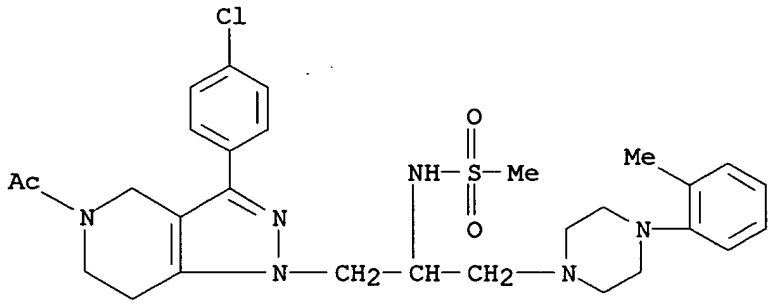
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Substituted pyrazoles I, methods of manufg. them, compns. contg. them, and methods of using them to treat, for example, autoimmune diseases mediated by cathepsin S, are described [R1 = H, N3, halo, alkoxy, OH, alkyl, alkenyl, cyano, NO2, (un)substituted NH2, acyl, etc.; R2 = H, halo, alkoxy, alkyl, alkenyl, haloalkyl, cyano, or (un)substituted NH2; or R1R2 = atoms to form (un)substituted (un)satd. (non)arom. 5- to 7-membered carbo- or heterocyclic ring; R3, R4 = H, alkyl; R5, R6 = H, alkyl, alkenyl, alkoxy, alkylthio, halo, or 4- to 7-membered carbo- or heterocyclyl; or R5R6 = atoms to form (un)substituted (un)satd. (non)arom. 5- to 7-membered carbo- or heterocyclic ring; n = 1 or 2; G = (un)substituted C3-6 alkanediyl or alkenediyl (substituents = OH, halo, oxo, aminoalkyl, etc.); X, Y, Z = N, (un)substituted CH; Ar = (un)substituted mono- or bicyclic (hetero)aryl; W = SO2, CO, (un)substituted CH2, bond; or WR1 = atoms to form a benzoxazol-2-yl, benzothiazol-2-yl, benzimidazol-2-yl, 1,2-benzisoxazol-3-yl, 1,2-benzisothiazol-3-yl, or 1,1-dioxo-1,2-benzothiazol-3-yl ring; including stereoisomers and pharmaceutically acceptable salts, esters, and amides]. Claimed usages include treatment of lupus, rheumatoid arthritis, and particularly asthma, and inhibition of tissue transplant rejection. Approx. 250 individual compds. I were prepd. and/or claimed, with detailed prepns. given for 24 compds. For instance, 4-(2-chloro-6-methanesulfonylaminophenyl)piperazine-1-carboxylic acid tert-Bu ester (prepd. in 4 steps) was deprotected with TFA and coupled with the corresponding epoxide (prepd. in several steps) to give title compd. II, a preferred compd. In an assay for inhibition of recombinant human cathepsin S in vitro, II had an IC50 of 0.06 .mu.M. Compd. III was another of three specifically preferred compds.

IT **400804-45-7P**, N-[2-[5-Acetyl-3-(4-chlorophenyl)-4,5,6,7-tetrahydropyrazolo[4,3-c]pyridin-1-yl]-1-(4-o-tolylpiperazin-1-ylmethyl)ethyl]methanesulfonamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of piperazinylpropyl-substituted pyrazolopyridines and analogs as cathepsin S inhibitors)

RN 400804-45-7 CAPLUS

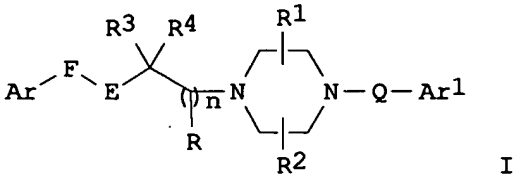
CN 1H-Pyrazolo[4,3-c]pyridine-1-ethanamine, 5-acetyl-3-(4-chlorophenyl)-4,5,6,7-tetrahydro-.alpha.-[[4-(2-methylphenyl)-1-piperazinyl]methyl]-N-(methylsulfonyl)- (9CI) (CA INDEX NAME)



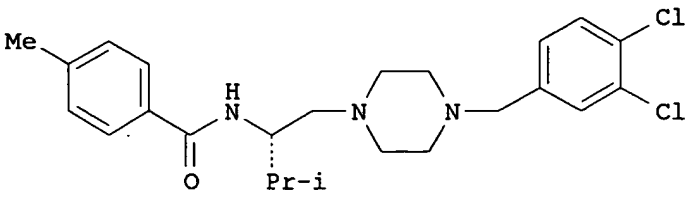
L8 ANSWER 24 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:43035 CAPLUS
DN 136:102404
TI Synthesis of disubstituted piperazinyl derivatives as CCR-3 receptor antagonists
IN Gong, Leyi; Kertesz, Denis John; Smith, David Bernard; Talamas, Francisco Xavier; Wilhelm, Robert Stephen
PA Syntex (U.S.A.) LLC, USA
SO U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 134,013.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 6339087 | B1 | 20020115 | US 1998-197282 | 19981120 |
| | US 6323223 | B1 | 20011127 | US 1998-134013 | 19980814 |
| | US 2003153577 | A1 | 20030814 | US 2001-942204 | 20010829 |
| | US 6770650 | B2 | 20040803 | | |
| | US 6683074 | B1 | 20040127 | US 2001-965068 | 20010926 |
| | US 2004266782 | A1 | 20041230 | US 2003-719204 | 20031121 |
| | US 6984637 | B2 | 20060110 | | |
| PRAI | US 1997-56001P | P | 19970818 | | |
| | US 1998-134013 | A2 | 19980814 | | |
| | US 1998-197282 | A3 | 19981120 | | |
| | US 2001-965068 | A3 | 20010926 | | |

OS MARPAT 136:102404
GI



I



II

AB Title compds. I [R1-2 = H, alkyl; m = 0-3; F = alkylene, alkenylene, bond; R = H, alkyl or R together with R4 and the atoms to which they are attached form a carbocycle; R3 = H; R4 = alkyl, haloalkyl, cycloalkyl, alkyl-SO0-2, alkylene-C(O)-Z, where Z = alkoxy, hydroxyalkyl; E = ureido, thioureido, amido, carboxamido,Ar = substituted aryl optionally

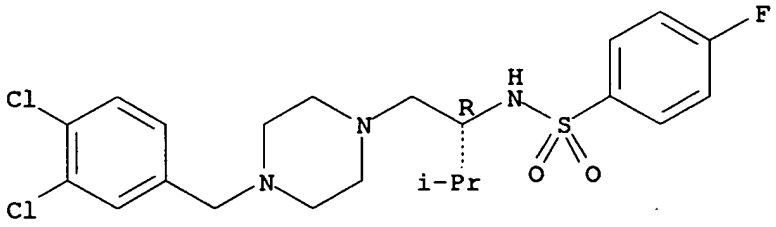
substituted with one, two or three alk(en)yl, alkoxy, haloalkoxy, halo, aryl, heteroaryl, etc.; Ar1 = (un)substituted aryl, optionally substituted with one, two or three alkyl, heteroalkyl, alkoxy, halo, haloalkyl, haloalkoxy, alkylthio, methylenedioxy, nitro, amino or a combination thereof; Q = alkylene-W, where W = bond, O, S, O2C, carboxamido or C(O)] were prepd. For example, N-Boc-piperazine was alkylated with 3,4-dichlorobenzyl bromide (CHCl3, Et3N, 1 h), deprotected (CHCl3, TFA, 1 h) and coupled to Boc-L-valine (CH2Cl2, EDCI, 2 h) to give the N-protected piperazinylamide intermediate. Deprotection (MeOH, HCl, 70.degree.C, 2.5 h) followed by amide redn. (THF, BH3, reflux, 2 h) and acylation with p-toluoyl chloride ( CH2Cl2, Et3N, 1 h) yielded II which was isolated as the dihydrochloride salt. The IC50 value (concn. of test compd. required to reduce 125I-eotaxin binding to the CCR-3 L 1.2 transfected cells by 50%) for selected compds. I was 0.24 - 3.52 .mu.M. Compds. I are useful in treating inflammatory or allergic diseases, e.g., asthma, allergic rhinitis, etc.

IT **220772-02-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of disubstituted piperazinyl derivs. as CCR-3 receptor antagonists)

RN 220772-02-1 CAPLUS

CN Benzenesulfonamide, N-[(1R)-1-[[4-[(3,4-dichlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]-4-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:31420 CAPLUS

DN 136:85815

TI Preparation of 2,3,4,5-tetrahydro-1H-3-benzazepine derivatives as GPR14 antagonists

IN Tarui, Naoki; Santo, Takashi; Watanabe, Hiroyuki; Aso, Kazuyoshi; Ishihara, Yuji

PA Takeda Chemical Industries, Ltd., Japan

SO PCT Int. Appl., 217 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2002002530 | A1 | 20020110 | WO 2001-JP5784 | 20010704 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |

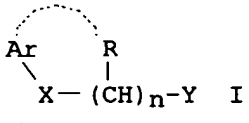
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| CA 2414976 | AA | 20020110 | CA 2001-2414976 | | 20010704 |
| AU 2001071018 | A5 | 20020114 | AU 2001-71018 | | 20010704 |
| JP 2002097142 | A2 | 20020402 | JP 2001-203519 | | 20010704 |
| EP 1310490 | A1 | 20030514 | EP 2001-949909 | | 20010704 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | | |
| US 2004063699 | A1 | 20040401 | US 2003-332023 | | 20030102 |
| PRAI JP 2000-206865 | A | 20000704 | | | |
| WO 2001-JP5784 | W | 20010704 | | | |

OS MARPAT 136:85815

GI



AB A G-protein-coupled receptor (GPR14) antagonist comprises compds. represented by the formula (I) or a salt thereof (wherein Ar represents optionally substituted aryl; X represents a spacer consisting of 1-4 atoms in the straight chain moiety; n is an integer of 1 to 10; R represents hydrogen or an optionally substituted hydrocarbon group, provided that R may be bonded to the substituent of Ar to form a ring; and Y represents optionally substituted amino or N-contg. heterocyclyl). These compds. are antagonists of orphan receptor GPR14 protein (urotensin II receptor) and are useful as inhibitors of vasoconstriction for the prevention or treatment of hypertension, arteriosclerosis, cardiac hypertrophy, myocardial infarction, or heart failure. Thus, a mixt. of 4-bromo-1-[3-(2,2,2-trifluoroacetyl)-2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl]-1-butanone, 1-phenylpiperazine, K2CO3, and DMF was stirred at 80.degree. for 2 h, followed by treatment of the product with a mixt. of 1 M aq. KOH and methanol and then with 1 N HCl/EtOAc to give 4-(4-phenyl-1-piperazinyl)-1-(2,3,4,5-tetrahydro-1H-3-benzazepin-7-yl)-1-butanone trihydrochloride (II). N-(2-{4-[bis(4-fluorophenyl)methyl]piperazin-1-yl}ethyl)-2,3,4,5-tetrahydro-1H-3-benzazepine-7-carboxamide trihydrochloride in vitro showed IC50 of 1.7 nM for inhibiting the binding of [125I]urotensin to human GPR14. A capsule and a tablet formulation contg. II were prepd.

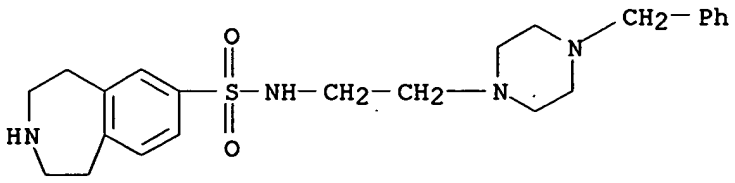
IT **387875-92-5P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of tetrahydrobenzazepine derivs. as GPR14 antagonists and vasoconstriction inhibitors for treatment and prevention of hypertension, arteriosclerosis, cardiac hypertrophy, myocardial infarction, or heart failure)

RN 387875-92-5 CAPLUS

CN 1H-3-Benzazepine-7-sulfonamide, 2,3,4,5-tetrahydro-N-[2-[4-(phenylmethyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

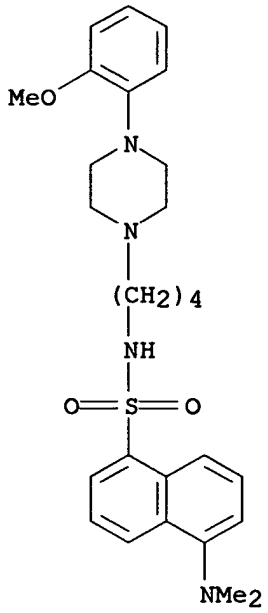


RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:656233 CAPLUS
DN 136:113011
TI Identification of the dopamine autoreceptor in the guinea-pig retina as D2 receptor using novel subtype-selective antagonists
AU Weber, Bernd; Schlicker, Eberhard; Sokoloff, Pierre; Stark, Holger
CS Institut fur Pharmakologie und Toxikologie, Universitat Bonn, Bonn, 53113, Germany
SO British Journal of Pharmacology (2001), 133(8), 1243-1248
CODEN: BJPCBM; ISSN: 0007-1188
PB Nature Publishing Group
DT Journal
LA English
AB 1 Dopamine release in the retina is subject to modulation via autoreceptors, which belong to the D2 receptor family (encompassing the D2, D3 and D4 receptors). The aim of the present study was to det. the receptor subtype (D2 vs. D3) involved in the inhibition of dopamine release in guinea-pig retinal disks, using established (haloperidol, (S)-nafadotride) and novel dopamine receptor antagonists (ST-148, ST-198). 2 HD2L and hD3 receptors were expressed in CHO cells and the pKi values detd. in binding studies with [125I]-iodosulpride were: haloperidol 9.22 vs. 8.54; ST-148 7.85 vs. 6.60; (S)-nafadotride 8.52 vs. 9.51; ST-198 6.14 vs. 7.92. 3 The elec. evoked tritium overflow from retinal disks preincubated with [3H]-noradrenaline (which represents quasi-physiol. dopamine release) was inhibited by the dopamine receptor agonists B-HT 920 (talipexole) and quinpirole (maximally by 82 and 71%; pEC50 5.80 and 5.83). The concn.-response curves of these agonists were shifted to the right by haloperidol (apparent pA2 8.69 and 8.23) and ST-148 (7.52 and 7.66). (S)-Nafadotride 0.01 .mu.M and ST-198 0.32 .mu.M did not affect the concn.-response curve of B-HT 920. 4 The dopamine autoreceptor in the guinea-pig retina can be classified as a D2 receptor. ST-148 and ST-198 show an improved selectivity for D2 and D3 receptors when compared to haloperidol and (S)-nafadotride, resp.
IT **390803-40-4**, ST 148
RL: PAC (Pharmacological activity); BIOL (Biological study)
(identification of the dopamine autoreceptor in the guinea-pig retina as D2 receptor using novel subtype-selective antagonists)
RN 390803-40-4 CAPLUS
CN 1-Naphthalenesulfonamide, 5-(dimethylamino)-N-[4-[4-(2-methoxyphenyl)-1-piperazinyl]butyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

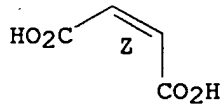
CRN 390803-39-1
CMF C27 H36 N4 O3 S



CM 2

CRN 110-16-7
CMF C4 H4 O4

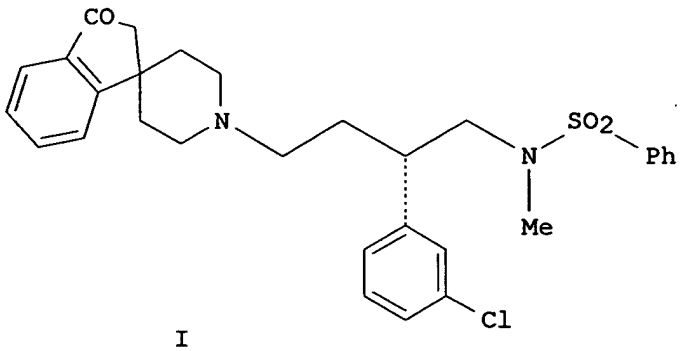
Double bond geometry as shown.



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:651007 CAPLUS
DN 136:47963
TI Antagonists of the human CCR5 receptor as anti-HIV-1 agents. Part 3: A proposed pharmacophore model for 1-[N-(methyl)-N-(phenylsulfonyl)amino]-2-(phenyl)-4-[4-(substituted)piperidin-1-yl]butanes
AU Finke, P. E.; Meurer, L. C.; Oates, B.; Shah, S. K.; Loebach, J. L.; Mills, S. G.; MacCoss, M.; Castonguay, L.; Malkowitz, L.; Springer, M. S.; Gould, S. L.; DeMartino, J. A.
CS Department of Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(18), 2469-2473
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.

DT Journal
LA English
OS CASREACT 136:47963
GI



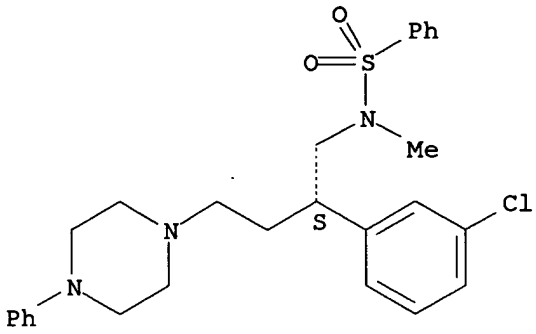

I

AB Structure-activity relationship studies directed toward the optimization of (2S)-2-(3-chlorophenyl)-1-[N-(methyl)-N-(phenylsulfonyl)amino]-4-[4-(substituted)piperidin-1-yl]butanes as CCR5 antagonists resulted in the synthesis of the spiro-indanone deriv. I (IC50=5 nM). These and previous results are summarized in a proposed pharmacophore model for this class of CCR5 antagonist.

IT **209160-71-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phenylsulfonylamino piperidinylbutanes as CCR5 receptor antagonists and potential anti-HIV-1 agents)

RN 209160-71-4 CAPLUS
CN Benzenesulfonamide, N-[(2S)-2-(3-chlorophenyl)-4-(4-phenyl-1-piperazinyl)butyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:432889 CAPLUS

DN 135:46173
TI Preparation of 4-phenyl-2-thiazolylalkyl-1,4-dihydropyridine-3,5-dicarboxylates and analogs as bradykinin antagonists
IN Kawai, Makoto; Murase, Noriaki; Ikeda, Takafumi; Shishido, Yuji; Nukui, Seiji; Okumura, Yoshiyuki; Kawamura, Mitsuhiro
PA Pfizer Inc., USA
SO Eur. Pat. Appl., 60 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

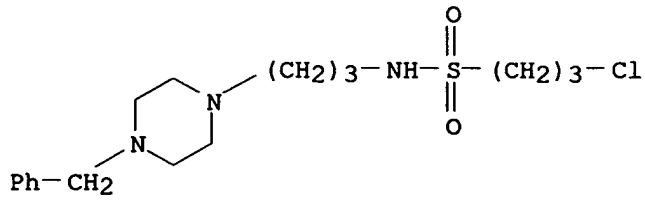
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 1106614 | A1 | 20010613 | EP 2000-310793 | 20001205 |
| | EP 1106614 | B1 | 20040107 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | AT 257479 | E | 20040115 | AT 2000-310793 | 20001205 |
| | PT 1106614 | T | 20040430 | PT 2000-310793 | 20001205 |
| | ES 2211460 | T3 | 20040716 | ES 2000-310793 | 20001205 |
| | JP 2001187793 | A2 | 20010710 | JP 2000-373447 | 20001207 |
| | JP 3651885 | B2 | 20050525 | | |
| | US 2001046993 | A1 | 20011129 | US 2000-731995 | 20001207 |
| | US 6444677 | B2 | 20020903 | | |
| | CA 2327925 | AA | 20010610 | CA 2000-2327925 | 20001208 |
| | BR 2000006371 | A | 20010724 | BR 2000-6371 | 20001211 |
| | JP 2005120107 | A2 | 20050512 | JP 2004-364980 | 20041216 |
| PRAI | US 1999-170142P | P | 19991210 | | |
| | JP 2000-373447 | A3 | 20001207 | | |

OS MARPAT 135:46173
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. (I) [wherein A = independently halo; Y1 = (CH2)m, CO, or SO; Y2 = N or CH; R1 and R2 = independently alkyl; R3 = (un)substituted (CH2)pcycloalkyl, or (bicyclo)alkyl; R4 = (un)substituted thiazolyl, imidazolyl, or oxazolyl; X = S, NH, alkylimino, or O; R5 = H or alkyl; R6 = alkyl or halo; m = 0-2; n = 0-5; p = 0-6; or the pharmaceutically acceptable salts thereof] were prepd. as bradykinin antagonists for the treatment of inflammation, asthma, allergic rhinitis, pain, etc. For example, II was synthesized in a multi-step sequence involving the reaction of Me 3-(2,6-dichlorophenyl)-2-[3-(1,3-thiazol-2-yl)propanoyl]-2-propenoate with di-Me 3-amino-2-pentenedioate to give the 2-(2-methoxy-2-oxoethyl)-1,5-dihydropyridine-3,5-dicarboxylate (85%), which was converted to the 3,5-bis(methoxycarbonyl)-1,4-dihydro-2-pyridinylacetic acid deriv. (80%) and amidated with 1-(1-piperazinylmethyl)cyclohexanecarbonitrile. In recombinant human bradykinin B2 receptor expressing CHO-K1 cells, I inhibited the binding of bradykinin to its receptor sites with IC50 values of 1 nM to 50 nM.
IT **344616-86-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-phenyl-2-thiazolylalkyl-1,4-dihydropyridine-3,5-dicarboxylates and analogs by reaction of benzylidenes with enamines as

bradykinin antagonists)
RN 344616-86-0 CAPLUS
CN 1-Propanesulfonamide, 3-chloro-N-[3-[4-(phenylmethyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)

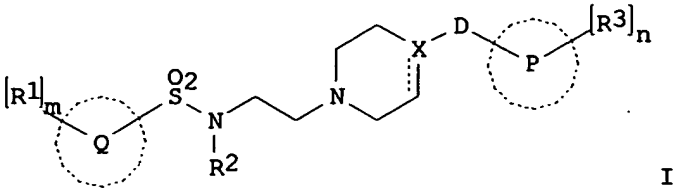


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

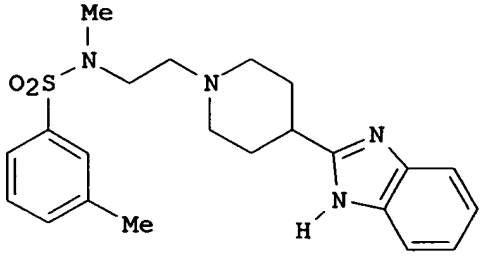
L8 ANSWER 29 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:688218 CAPLUS
DN 133:252456
TI Preparation of N-[2-piperazino(or piperidino)ethyl] benzenesulfonamides and thiophenesulfonamides as 5-HT7 receptor antagonists
IN Lovell, Peter John
PA Smithkline Beecham Plc, UK
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000056712 | A1 | 20000928 | WO 2000-EP2267 | 20000314 |
| | W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1163221 | A1 | 20011219 | EP 2000-916945 | 20000314 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | US 6660751 | B1 | 20031209 | US 2001-937043 | 20010920 |
| PRAI | GB 1999-6624 | A | 19990323 | | |
| | WO 2000-EP2267 | W | 20000314 | | |

OS MARPAT 133:252456
GI



I



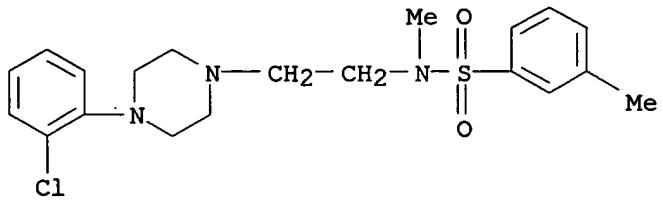
II

AB The title compds. [I; Q = Ph, thienyl; R1 = halo, OH, alkyl, etc.; m = 0-3; R2 = alkyl; X = N, C, CH; D = a single bond; CO, O, CH2 subject to the proviso that when X = N then D is not O; P = Ph, naphthyl, 5-6 membered heteroaryl contg. 1-3 heteroatoms selected from O, N and S, etc.; R3 = (un)substituted alkyl; n = 0-3] having 5-HT7 receptor antagonist activity, and therefore useful in the treatment of CNS and other disorders, were prepd. E.g., a multi-step synthesis of benzenesulfonamide II was given. All compds. I tested had a pKi of 6.2-9.0 against 5-HT7 receptor binding.

IT **295790-23-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-[2-piperazino(or piperidino)ethyl] benzenesulfonamides and thiophenesulfonamides as 5-HT7 receptor antagonists)

RN 295790-23-7 CAPLUS

CN Benzenesulfonamide, N-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

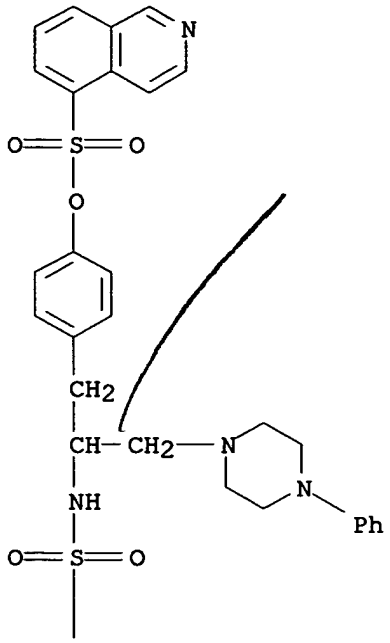


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

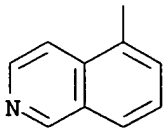
L8 ANSWER 30 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:405009 CAPLUS

DN 133:172107
TI Antagonist effects on human P2X7 receptor-mediated cellular accumulation of YO-PRO-1
AU Michel, A. D.; Kaur, R.; Chessell, I. P.; Humphrey, P. P. A.
CS Glaxo Institute of Applied Pharmacology, Department of Pharmacology, University of Cambridge, Cambridge, CB2 1QJ, UK
SO British Journal of Pharmacology (2000), 130(3), 513-520
CODEN: BJPCBM; ISSN: 0007-1188
PB Nature Publishing Group
DT Journal
LA English
AB 1 The authors have examd. the interaction of P2 antagonists with the human P2X7 receptor by studying their effect on 2' and 3'-O-benzoyl-benzoyl-ATP (DbATP) stimulated cellular accumulation of the fluorescent, DNA binding dye, YO-PRO-1 (MW = 375 Da). 2 In suspensions of HEK293 cells expressing human recombinant P2X7 receptors, DbATP produced time and concn.-dependent increases in YO-PRO-1 fluorescence. This response presumably reflects YO-PRO-1 entry through P2X7 receptor channels and binding to nucleic acids. When studies were performed in a NaCl-free, sucrose-contg. buffer, full concn.-effect curves to DbATP could be constructed. 3 The P2 antagonists, pyridoxalphosphate-6-azophenyl-2',4'-disulfonic acid (PPADS) and periodate oxidized ATP (oATP), reduced the potency of DbATP and decreased its max. response. 1-[N,O-bis(1,5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (KN62) and its analog, KN04, reduced the potency of DbATP. Schild slopes for KN62 and KN04 were shallow and exhibited a plateau at concns. of compd. greater than 1 .mu.M, indicating that these compds. were not competitive antagonists. 4 Calmidazolium and a monoclonal antibody to human P2X7 receptors attenuated DbATP-stimulated YO-PRO-1 accumulation but they were not competitive antagonists and only produced 2-3 fold decreases in the potency of DbATP. 5 The effects of PPADS and KN62 were partially reversible whereas those of oATP were not. PPADS protected cells against the irreversible antagonist effects of oATP suggesting a common site of action. In contrast KN62 was not effective suggesting that it may bind at a different site to oATP and PPADS. 6 This study has demonstrated that P2X7 receptor function can be quantified by measuring DbATP stimulated YO-PRO-1 accumulation and has provided addnl. information about the interaction of P2 receptor antagonists with the human P2X7 receptor.
IT **129695-80-3**, KN04
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist effects on human P2X7 receptor-mediated cellular accumulation of fluorescent dye YO-PRO-1 stimulated by O-benzoyl-benzoyl-ATP)
RN 129695-80-3 CAPLUS
CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

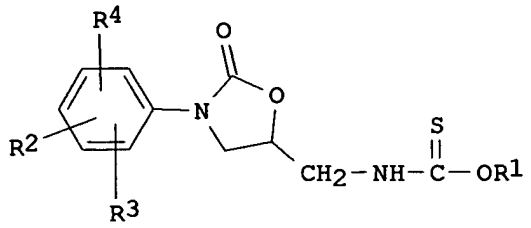
L8 ANSWER 31 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:335397 CAPLUS
DN 132:334453
TI Preparation of oxazolidinylmethylthiocarbamic acid derivatives as antibacterial agents
IN Kado, Noriyuki; Tokuyama, Ryukou; Tsubouchi, Masatoshi; Tomita, Yayoi
PA Hokuriku Seiyaku Co., Ltd., Japan
SO PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000027830 | A1 | 20000518 | WO 1999-JP6260 | 19991110 |

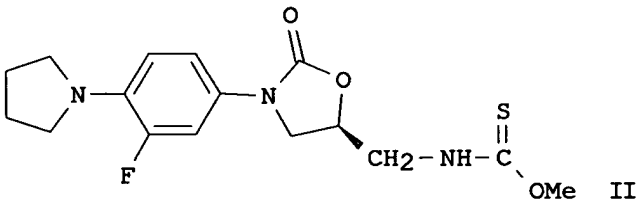
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,

IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

JP 2000204084 A2 20000725 JP 1999-273230 19990927
EP 1130016 A1 20010905 EP 1999-971804 19991110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRAI JP 1998-320137 A 19981111
JP 1999-273230 A 19990927
WO 1999-JP6260 W 19991110
OS MARPAT 132:334453
GI



I



II

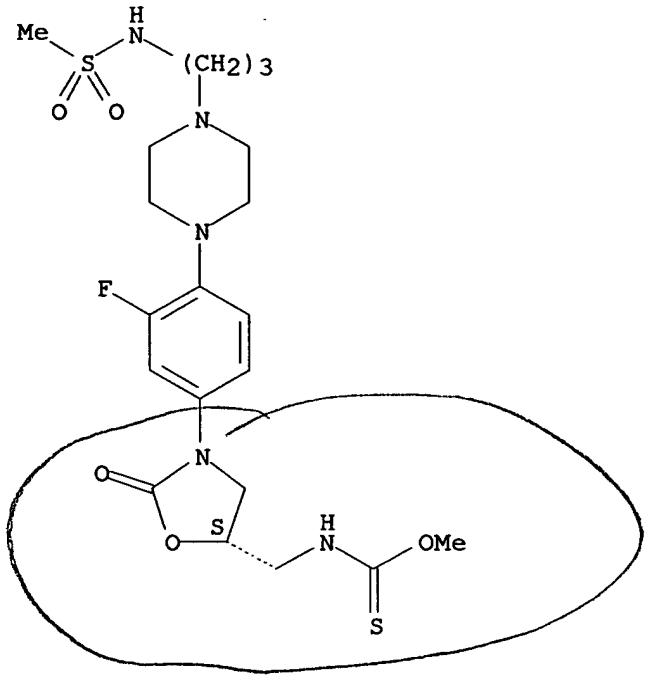
AB The title compds. I [R1 is optionally substituted alkyl or optionally substituted cycloalkyl; and R2, R3 and R4 are each independently hydrogen, halogeno, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted amino, optionally substituted alkanoyl, optionally substituted cycloalkyloxy contg. a heteroatom as the ring-constituting atom, or an optionally substituted satd. heterocyclic group, or alternatively any two of R2, R3 and R4 together with the benzene ring may form an optionally substituted fused hydrocarbon ring] are prepd. The title compd. II in vitro showed IC50 of 0.39 .mu.g/mL against S. aureus, vs. IC50 of 3.13 .mu.g/mL for linezolid.

IT **268208-72-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of oxazolidinylmethylthiocarbamic acid derivs. as antibacterial agents)

RN 268208-72-6 CAPLUS
CN Carbamothioic acid, [[(5S)-3-[3-fluoro-4-[4-[3-

[(methylsulfonyl)amino]propyl]-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-, O-methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 32 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:456816 CAPLUS
DN 131:226612
TI 1-[N,O-Bis-(5-isoquinolinesulphonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (KN-62), an inhibitor of calcium-dependent calmodulin protein kinase II, inhibits both insulin- and hypoxia-stimulated glucose transport in skeletal muscle
AU Brozinick, Joseph T., Jr.; Reynolds, Thomas H.; Dean, David; Cartee, Gregory; Cushman, Samuel W.
CS Experimental Diabetes, Metabolism and Nutrition Section, DB/NIDDK National Institutes of Health, Bethesda, MD, 20892, USA
SO Biochemical Journal (1999), 339(3), 533-540
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English
AB Previous studies have indicated a role for calmodulin in hypoxia- and insulin-stimulated glucose transport. However, since calmodulin interacts with multiple protein targets, it is unknown which of these targets is involved in the regulation of glucose transport. In the present study, we have used the calcium-dependent calmodulin protein kinase II (CAMKII) inhibitor 1-[N,O-bis-(5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (KN-62) to investigate the possible role of this enzyme in the regulation of glucose transport in isolated rat soleus and epitrochlearis muscles. KN-62 did not affect basal 2-deoxyglucose transport, but it did inhibit both insulin- and hypoxia-stimulated glucose

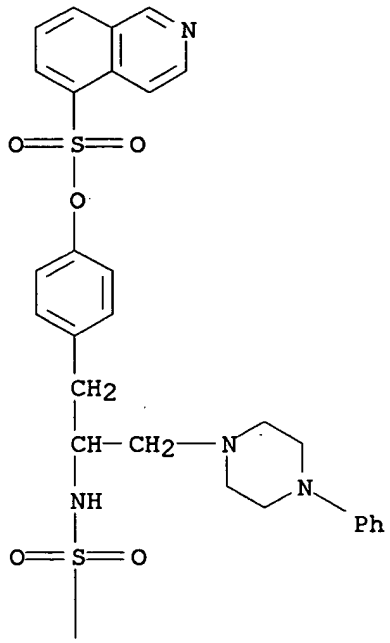
transport activity by 46 and 40% resp. 1-[N,O-Bis-(1,5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (KN-04), a structural analog of KN-62 that does not inhibit CAMKII, had no effect on hypoxia- or insulin-stimulated glucose transport. Accordingly, KN-62 decreased the stimulated cell-surface GLUT4 labeling by a similar extent as the inhibition of glucose transport (insulin, 49% and hypoxia, 54%). Addnl. expts. showed that KN-62 also inhibited insulin- and hypoxia-stimulated transport by 37 and 40% resp. in isolated rat epitrochlearis (a fast-twitch muscle), indicating that the effect of KN-62 was not limited to the slow-twitch fibers of the soleus. The inhibitory effect of KN-62 on hypoxia-stimulated glucose transport appears to be specific to CAMKII, since KN-62 did not inhibit hypoxia-stimulated 45Ca efflux from muscles pre-loaded with 45Ca, or hypoxia-stimulated glycogen breakdown. Addnl., KN-62 affected neither insulin-stimulated phosphoinositide 3-kinase nor Akt activity, suggesting that the effects of KN-62 are not due to non-specific effects of this inhibitor on these regions of the insulin-signalling cascade. The results of the present study suggest that CAMKII might have a distinct role in insulin- and hypoxia-stimulated glucose transport, possibly in the vesicular trafficking of GLUT4.

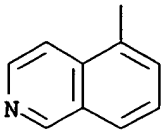
IT **129695-80-3**, KN-04
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of insulin- and hypoxia-stimulated glucose transport in skeletal muscle by inhibitor of calcium-dependent calmodulin protein kinase II)

RN 129695-80-3 CAPLUS

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



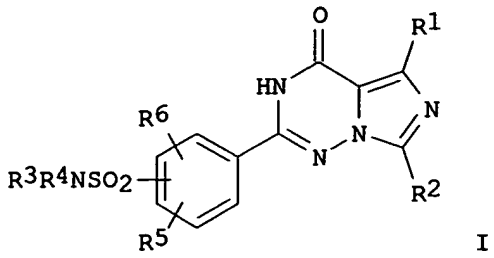


RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 33 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:325936 CAPLUS
DN 130:352283
TI Preparation of 2-phenylimidazotriazinones as phosphodiesterase inhibitors.
IN Niewohner, Ulrich; Es-Sayed, Mazen; Haning, Helmut; Schenke, Thomas; Schlemmer, Karl-Heinz; Keldenich, Jorg; Bischoff, Erwin; Perzborn, Elisabeth; Dembowsky, Klaus; Serno, Peter; Nowakowski, Marc
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 329 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9924433 | A1 | 19990520 | WO 1998-EP6910 | 19981031 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | DE 19750085 | A1 | 19990520 | DE 1997-19750085 | 19971112 |
| | DE 19812462 | A1 | 19990930 | DE 1998-19812462 | 19980323 |
| | DE 19840289 | A1 | 20000309 | DE 1998-19840289 | 19980904 |
| | CA 2309332 | AA | 19990520 | CA 1998-2309332 | 19981031 |
| | CA 2309332 | C | 20021203 | | |
| | CA 2395558 | AA | 19990520 | CA 1998-2395558 | 19981031 |
| | AU 9915587 | A1 | 19990531 | AU 1999-15587 | 19981031 |
| | AU 738675 | B2 | 20010920 | | |
| | TR 200001338 | T2 | 20000821 | TR 2000-200001338 | 19981031 |
| | GB 2346877 | A1 | 20000823 | GB 2000-10974 | 19981031 |
| | GB 2346877 | B2 | 20011205 | | |
| | BR 9812785 | A | 20001010 | BR 1998-12785 | 19981031 |
| | EP 1049695 | A1 | 20001108 | EP 1998-959821 | 19981031 |
| | EP 1049695 | B1 | 20020213 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | EE 200000291 | A | 20010615 | EE 2000-291 | 19981031 |
| | NZ 504436 | A | 20010831 | NZ 1998-504436 | 19981031 |
| | JP 2001522851 | T2 | 20011120 | JP 2000-520443 | 19981031 |
| | JP 3356428 | B2 | 20021216 | | |
| | EP 1174431 | A2 | 20020123 | EP 2001-123321 | 19981031 |

| | | | | | |
|---|---|---|---|---|---|
| | EP 1174431 | A3 | 20020130 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | DE 19881732 | C1 | 20020131 | DE 1998-19881732 | 19981031 |
| | AT 213246 | E | 20020215 | AT 1998-959821 | 19981031 |
| | PT 1049695 | T | 20020731 | PT 1998-959821 | 19981031 |
| | ES 2172945 | T3 | 20021001 | ES 1998-959821 | 19981031 |
| | JP 2002348290 | A2 | 20021204 | JP 2002-130480 | 19981031 |
| | CN 1123573 | B | 20031008 | CN 1998-811092 | 19981031 |
| | ES 2194567 | A1 | 20031116 | ES 2000-200050033 | 19981031 |
| | ES 2194567 | B1 | 20050301 | | |
| | CH 693954 | A | 20040514 | CH 2000-932 | 19981031 |
| | CN 1508137 | A | 20040630 | CN 2003-2003119940 | 19981031 |
| | RU 2260593 | C2 | 20050920 | RU 2000-115281 | 19981031 |
| | IN 188419 | A | 20020921 | IN 1998-DE3276 | 19981105 |
| | ZA 9810297 | A | 19990520 | ZA 1998-10297 | 19981111 |
| | TW 513431 | B | 20021211 | TW 1998-87118724 | 19981111 |
| | LU 90561 | A1 | 20001201 | LU 2000-90561 | 20000405 |
| | BG 104406 | A | 20010831 | BG 2000-104406 | 20000505 |
| | FI 2000001086 | A | 20000509 | FI 2000-1086 | 20000509 |
| | FI 113772 | B1 | 20040615 | | |
| | NO 2000002444 | A | 20000511 | NO 2000-2444 | 20000511 |
| | NO 314940 | B1 | 20030616 | | |
| | SE 2000001745 | A | 20000511 | SE 2000-1745 | 20000511 |
| | SE 522809 | C2 | 20040309 | | |
| | HR 2000000292 | A1 | 20010430 | HR 2000-292 | 20000511 |
| | MX 200004634 | A | 20001110 | MX 2000-4634 | 20000512 |
| | US 6362178 | B1 | 20020326 | US 2000-554162 | 20000721 |
| | HK 1031730 | A1 | 20041015 | HK 2001-102357 | 20010402 |
| | US 6566360 | B1 | 20030520 | US 2001-943530 | 20010830 |
| | NO 2002001714 | A | 20000511 | NO 2002-1714 | 20020411 |
| | US 2004067945 | A1 | 20040408 | US 2003-365740 | 20030212 |
| | US 6890922 | B2 | 20050510 | | |
| | US 2005070541 | A1 | 20050331 | US 2004-923544 | 20040820 |
| PRAI | DE 1997-19750085 | A | 19971112 | | |
| | DE 1998-19812462 | A | 19980323 | | |
| | DE 1998-19840289 | A | 19980904 | | |
| | CA 1998-2309332 | A3 | 19981031 | | |
| | EP 1998-959821 | A3 | 19981031 | | |
| | JP 2000-520443 | A3 | 19981031 | | |
| | WO 1998-EP6910 | W | 19981031 | | |
| | NO 2000-2444 | A | 20000511 | | |
| | US 2000-554162 | A1 | 20000721 | | |
| | US 2001-943530 | A1 | 20010830 | | |
| | US 2003-365740 | A1 | 20030212 | | |
| OS | MARPAT 130:352283 | | | | |
| GI | | | | | |



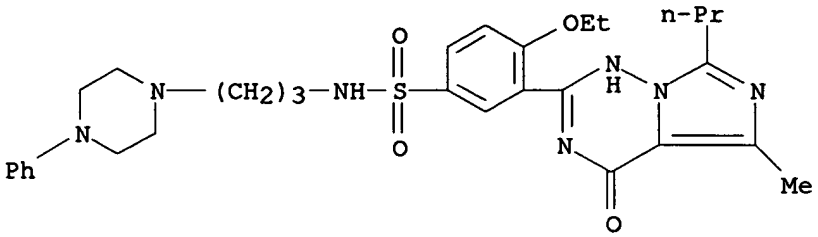
I

AB Title compds. [I; R1 = H, alkyl; R2 = alkyl; R3, R4 = H, alkenyl, alkoxy, (substituted) (O-interrupted) alkyl, amino, adamantyl, cycloalkyl, etc.; NR3R4 = 5-7 membered (benzo-fused) (unsatd.) heterocyclyl, etc.; R5, R6 = H, alkyl, OH, alkoxy], were prepd. as cGMP-metabolizing phosphodiesterases for treating cardiovascular and cerebrovascular diseases and/or diseases of the urogenital system, esp. for treating erectile dysfunction. Thus, 4-ethoxy-3-(5,7-dimethyl-4-oxo-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)benzenesulfonyl chloride (prepn. given) in CH2Cl2 was treated with DMAP and N-methylpiperazine at 0.degree. followed by stirring overnight to give 34.5% 2-[2-ethoxy-5-(4-methylpiperazin-1-ylsulfonyl)phenyl]-5,7-dimethyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one. I inhibited phosphodiesterase V with IC50 = 1-10 nM.

IT **224787-56-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-phenylimidazotriazinones as phosphodiesterase inhibitors)

RN 224787-56-8 CAPLUS

CN Benzenesulfonamide, 3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxy-N-[3-(4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



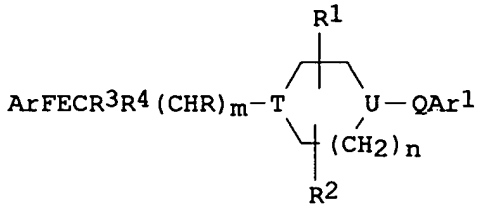
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 34 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:147946 CAPLUS
DN 130:196670
TI Arylcarbamoylalkylpiperazines and -piperidines as CCR-3-receptor antagonists
IN Gong, Leyi; Kertesz, Denis John; Smith, David Bernard; Talamas, Francisco Xavier; Wilhelm, Robert Stephen
PA F. Hoffmann-La Roche A.-G., Switz.
SO Ger. Offen., 60 pp.

CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE 19837386 | A1 | 19990225 | DE 1998-19837386 | 19980818 |
| | EP 903349 | A2 | 19990324 | EP 1998-114971 | 19980810 |
| | EP 903349 | A3 | 20000524 | | |
| | EP 903349 | B1 | 20060104 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY | | | | |
| | NZ 331319 | A | 20000327 | NZ 1998-331319 | 19980811 |
| | CA 2245043 | AA | 19990218 | CA 1998-2245043 | 19980814 |
| | ES 2154167 | A1 | 20010316 | ES 1998-1760 | 19980814 |
| | ES 2154167 | B1 | 20011101 | | |
| | NO 9803749 | A | 19990219 | NO 1998-3749 | 19980817 |
| | GB 2330580 | A1 | 19990428 | GB 1998-17910 | 19980817 |
| | AU 9880800 | A1 | 19990225 | AU 1998-80800 | 19980818 |
| | AU 744059 | B2 | 20020214 | | |
| | FR 2767826 | A1 | 19990305 | FR 1998-10504 | 19980818 |
| | CN 1211572 | A | 19990324 | CN 1998-117990 | 19980818 |
| | CN 1107061 | B | 20030430 | | |
| | JP 11147872 | A2 | 19990602 | JP 1998-231918 | 19980818 |
| | JP 3014367 | B2 | 20000228 | | |
| | SG 70110 | A1 | 20000125 | SG 1998-3133 | 19980818 |
| | BR 9803179 | A | 20000328 | BR 1998-3179 | 19980818 |
| | IT 1304150 | B1 | 20010308 | IT 1998-MI1902 | 19980818 |
| | US 2004266782 | A1 | 20041230 | US 2003-719204 | 20031121 |
| | US 6984637 | B2 | 20060110 | | |
| PRAI | US 1997-56001P | P | 19970818 | | |
| | US 1998-134013 | A3 | 19980814 | | |
| | US 2001-965068 | A3 | 20010926 | | |

OS MARPAT 130:196670
GI




I

AB Title compds. I [Ar, Ar1 = aryl, heteroaryl; E = (un)substituted CONH, SO2NH, NHCONH, NHSO2NH, NHCSNH, NHCO, NHCO2, O2CNH, NHSO2; F = alkylene, alkenylene; R = H, alkyl; R1, R2 = H, alkyl; R3, R4 = H, (un)substituted alkyl, cycloalkyl, heterocyclic, CN; CR3R4 = carbocyclic, heterocyclic; RR3 = atoms required to form a carbocyclic or heterocyclic ring; Q = (un)substituted alkylene, heteroalkylene; one of T an U = N, the other is N or CH; n = 0-2] were prepd. for use as CCR-3 receptor antagonists, useful in treating asthma in particular. Thus, N-[(1S)-[4-(3,4-dichlorobenzyl)piperazin-1-ylmethyl]-2-methylpropyl]-4-methylbenzamide.2HCl was prepd. from 1-(3,4-dichlorobenzyl)piperazine and BOC-L-valine in 4 steps. This compd. had an IC50 for CCR-3 receptor

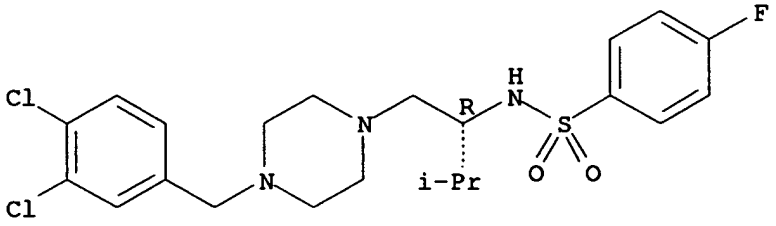
binding of 0.24 .mu.M.

IT **220772-02-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylcarbamoylalkylpiperazines and -piperidines as CCR-3-receptor antagonists)

RN 220772-02-1 CAPLUS

CN Benzenesulfonamide, N-[(1R)-1-[[4-[(3,4-dichlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]-4-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L8 ANSWER 35 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1998:486936 CAPLUS

DN 129:211964

TI Isoquinolines as antagonists of the P2X7 nucleotide receptor: high selectivity for the human versus rat receptor homologs

AU Humphreys, Benjamin D.; Virginio, Caterina; Surprenant, Annmarie; Rice, Janet; Dubyak, George R.

CS Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University, Cleveland, OH, 44106, USA

SO Molecular Pharmacology (1998), 54(1), 22-32
CODEN: MOPMA3; ISSN: 0026-895X

PB Williams & Wilkins

DT Journal

LA English

AB 1-[N,O-Bis(5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine (KN-62) and N-[1-[N-methyl-p-(5-isoquinolinesulfonyl)benzyl]-2-(4 phenylpiperazine)ethyl]-5-isoquinolinesulfonamide (KN-04) potently inhibit the human lymphocyte P2Z receptor, an ATP-gated cation channel [Br J Pharmacol 120:1483-1490 (1997)]. Although the mol. identity of the lymphocyte P2Z receptor has not been established, it shares many functional characteristics with the cloned P2X7, nucleotide receptor. We have tested whether these isoquinolines inhibit P2X receptor function in human embryonic kidney 293 cells that stably express the human or rat recombinant P2X7 receptors. ATP activation of cation currents and uptake of the org. dye ethidium were potently inhibited by KN-62 and KN-04 in human embryonic kidney cells expressing the human P2X7R but not the rat P2X7R, even though these species homologs share 80% amino acid identity. Introduction of the first 335 amino acids of the human P2X7R sequence conferred KN-62 sensitivity to the rat P2X7R; this suggests that isoquinolines interact with residues in the amino-terminal half (contg. the large extracellular loop) of the human P2X7R. KN-62 and KN-04 also potently inhibited ATP-gated Ca2+ influx and ethidium uptake in several leukocyte cell lines (THP-1, BAC1.2f5, and BW5147) that natively express the human or murine P2X7R mRNA. The ability of isoquinoline sulfonamides

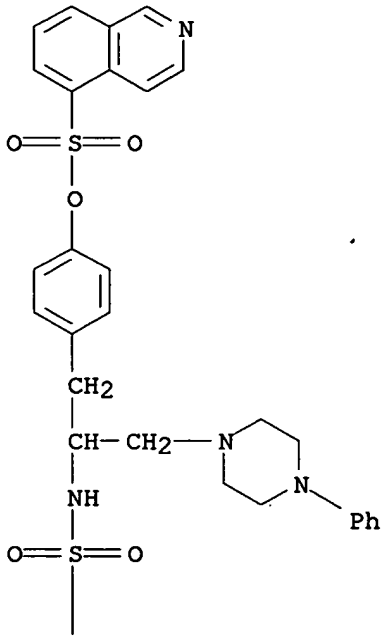
to potently inhibit human and murine P2X7R signaling will be a useful tool for identifying P2Z/P2X7 functional responses in other cell types. The substantial differences in pharmacol. sensitivity between rat and human P2X7R may also indicate structural domains important in channel/pore activation.

IT **129695-80-3**, KN-04
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(isoquinolines as antagonists of P2X7 nucleotide receptor and high selectivity for human vs. rat receptor homologs)

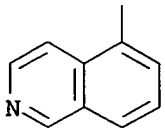
RN 129695-80-3 CAPLUS

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A



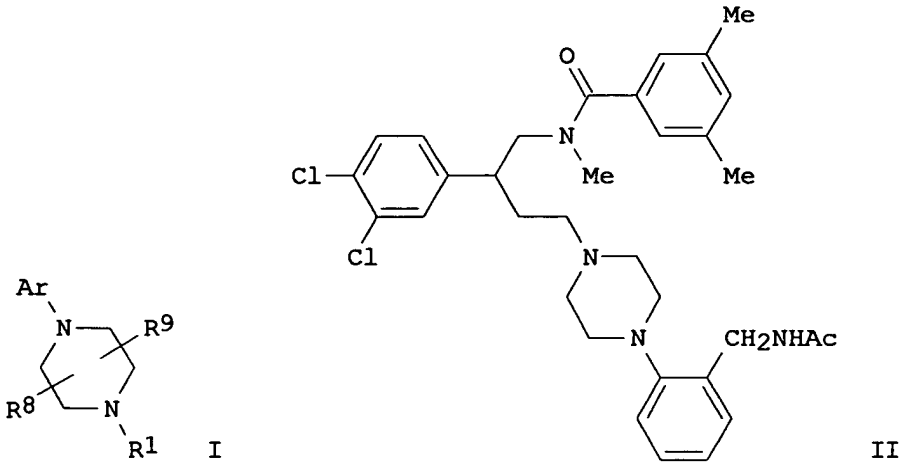

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 36 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:402315 CAPLUS

DN 129:81753
TI Preparation of substituted aryl piperazines as modulators of chemokine receptor activity
IN Mills, Sander G.; Springer, Martin S.; MacCoss, Malcolm
PA Merck & Co., Inc., USA; Mills, Sander G.; Springer, Martin S.; MacCoss, Malcolm
SO PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9825617 | A1 | 19980618 | WO 1997-US22769 | 19971212 |
| | W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9855224 | A1 | 19980703 | AU 1998-55224 | 19971212 |
| PRAI | US 1996-32889P | P | 19961213 | | |
| | US 1996-33567P | P | 19961220 | | |
| | WO 1997-US22769 | W | 19971212 | | |

OS MARPAT 129:81753
GI




AB The title compds. [I; R1 = (un)substituted C1-8 alkyl, C1-8 alkenyl; the nitrogen attached to R1 is optionally quaternized with C1-4 alkyl or phenylC1-4alkyl or is optionally present as N-oxide; Ar = (un)substituted Ph, pyridyl, pyrimidyl, etc.; R8, R9 = H, (un)substituted C1-4 alkyl], useful as modulators of chemokine receptor activity, were prepd. Thus, 5-step synthesis of the title compd. 3(S)-II starting from 3,5-dimethylbenzoic acid and 3(S)-(3,4-dichlorophenyl)-4-methylamino-1-pentene was described. In particular, compds. I are useful as modulators of the chemokine receptors CCR-1, CCR-2, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CXCR-3, and/or CXCR-4. Compds. I can be used for preventing

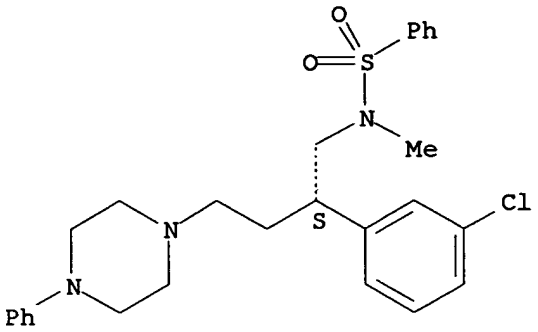
infection by HIV, treating infection by HIV, delaying of the onset of AIDS, or treating AIDS. Compds. I are effective at 0.1-5 mg/kg/day.

IT **209160-71-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted aryl piperazines as modulators of chemokine receptor activity)

RN 209160-71-4 CAPLUS

CN Benzenesulfonamide, N-[(2S)-2-(3-chlorophenyl)-4-(4-phenyl-1-piperazinyl)butyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 37 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1998:126254 CAPLUS

DN 128:204878

TI Preparation of pyrazinobenzothiazine derivatives and analogs for the treatment of inflammation and autoimmune diseases

IN Kaneko, Toshihiko; Clark, Richard; Ohi, Norihito; Ozaki, Fumihiro; Kawahara, Tetsuya; Kamada, Atsushi; Okano, Kazuo; Yokohama, Hiromitsu; Muramoto, Kenzo; Arai, Tohru; Ohkuro, Masayoshi; Takenaka, Osamu; Sonoda, Jiro

PA Eisai Co., Ltd., Japan

SO PCT Int. Appl., 1344 pp.
CODEN: PIXXD2

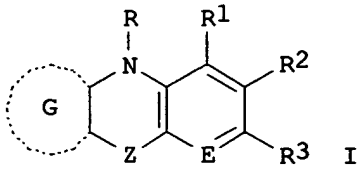
DT Patent

LA Japanese

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9806720 | A1 | 19980219 | WO 1997-JP2787 | 19970808 |
| W: AU, CA, CN, HU, JP, KR, MX, NO, NZ, RU, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2262569 | AA | 19980219 | CA 1997-2262569 | 19970808 |
| AU 9737849 | A1 | 19980306 | AU 1997-37849 | 19970808 |
| ZA 9707103 | A | 19990208 | ZA 1997-7103 | 19970808 |
| EP 934941 | A1 | 19990811 | EP 1997-934750 | 19970808 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| US 6518423 | B1 | 20030211 | US 1999-230852 | 19990405 |
| US 2004092737 | A1 | 20040513 | US 2002-247310 | 20020920 |

PRAI JP 1996-210344 A 19960809
WO 1997-JP2787 W 19970808
US 1999-230852 A3 19990405
OS MARPAT 128:204878
GI

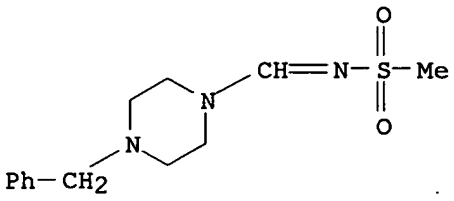


I

AB The title compds. I [R1 to R3 are the same or different and each represents hydrogen, optionally substituted lower alkyl, optionally substituted cycloalkyl, etc., provided that when R1 to R3 are all optionally substituted lower alkyl groups, they do not simultaneously represent Me groups; R represents hydrogen, lower alkyl, etc.; E represents N, C, etc.; Z represents O, S, SO, SO2, etc.; and the ring G represents an optionally substituted heteroaryl ring having at least one nitrogen atom] are prepd. I are useful in the treatment and prevention of inflammatory immunol. diseases, autoimmune diseases, rheumatism, collagen disease, asthma, nephritis, ischemic reflow disorders, psoriasis, atopic dermatitis or rejection reactions following organ transplantation. The compd. (syn)-[3-(10H-pyrazino[2,3-b][1,4]benzothiazin-8-ylmethyl)-3-azabicyclo[3.3.1]nona-9-yl]acetic acid (II) at 10 mg/kg orally gave 65% inhibition of carrageenin-induced inflammation in rats. II in vitro showed IC50 of 2.3 .mu.M against the expression of ICAM-1.

IT **203663-09-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pyrazinobenzothiazine derivs. and analogs for treatment of inflammation and autoimmune diseases)

RN 203663-09-6 CAPLUS
CN Methanesulfonamide, N-[[4-(phenylmethyl)-1-piperazinyl]methylene]- (9CI) (CA INDEX NAME)

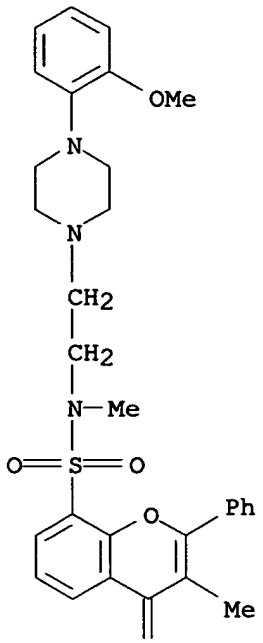


RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 38 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:713805 CAPLUS
DN 128:18928
TI Antagonism to noradrenaline-induced lethality in rats is related to affinity for the .alpha.1A-adrenoceptor subtype

AU Testa, Rodolfo; Guarneri, Luciano; Ibba, Marina; Angelico, Patrizia; Poggesi, Elena; Taddei, Carlo; Motta, Gianni; Leonardi, Amedeo
CS Pharmaceutical RandD Division, RECORDATI S.p.A., Milan, 20148, Italy
SO Life Sciences (1997), 61(22), 2177-2188
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier
DT Journal
LA English
AB The potency of several .alpha.1-adrenoceptor antagonists in preventing the noradrenaline-induced lethality in conscious rats, their binding affinity for the native .alpha.1A- and .alpha.1B-adrenoceptors, the recombinant animal .alpha.1a-, .alpha.1b- and .alpha.1d-adrenoceptor subtypes, as well as their functional affinity for the .alpha.1L-adrenoceptor subtype were evaluated. The potency of the tested compds. as antagonists of noradrenaline-induced lethality was correlated with the affinity for the .alpha.1A- (and .alpha.1a-) adrenoceptor subtype, but not with the affinity for the other subtypes. On the contrary, the hypotensive effects of the compds., assessed in anesthetized rats, were not clearly related with the affinity for any of the .alpha.1-subtypes. These results suggest that the .alpha.1A-subtype plays a detg. role in preventing lethality induced by noradrenaline in the rats, and that this activity is unrelated to the hypotensive effect of the compds., which cannot be clearly correlated with affinity for a particular .alpha.1-adrenoceptor subtype.
IT **152735-60-9**, Rec 15/2757
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antagonism to noradrenaline-induced lethality relation to affinity for .alpha.1A-adrenoceptor subtype)
RN 152735-60-9 CAPLUS
CN 4H-1-Benzopyran-8-sulfonamide, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N,3-dimethyl-4-oxo-2-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A


● HCl

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 39 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:686837 CAPLUS
DN 128:3594
TI A series of quinoline-2-carboxylic acid derivatives: new potent glycine site NMDA receptor antagonists
AU Kim, Ran Hee; Choi, Jin Li; Choi, Seung Won; Lee, Kwang Sook; Jung, Young Sik; Park, Woo Kyu; Seong, Churl Min; Park, No Sang
CS Korea Research Institute of Chemical Technology, Taejeon, 305-606, S. Korea
SO Bulletin of the Korean Chemical Society (1997), 18(9), 939-945
CODEN: BKCSDE; ISSN: 0253-2964
PB Korean Chemical Society
DT Journal
LA English
GI

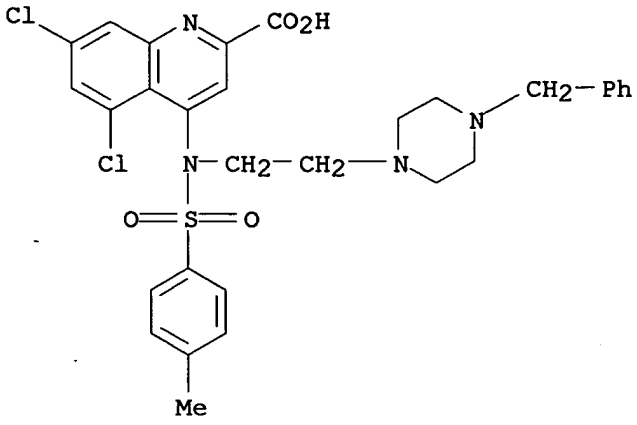
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Several types of 4-substituted-quinoline-2-carboxylic acid derivs. possessing different substituents at C4-position such as sulfonyl, phosphonyl, carbonyl groups, or a flexible alkyl chain have been synthesized and evaluated for their in vitro antagonistic activity at the glycine site on the N-methyl-D-aspartate (NMDA) receptor. Of them, 5,7-dichloro-4-(tolylsulfonylamino)-quinoline-2-carboxylic acid was found to have the best in vitro binding affinity with IC50 of 0.57 .mu.M. On the other hand, in quinolinecarboxylic acids I and II (n = 1, 2) the introduction of flexible alkyl chains on C4 of the quinoline mother nuclei caused a significant decrease of the in vitro binding affinity. In addn., replacement of polar carboxylic acid group on C2 by neutral bioisosteres in quinolinic amides III (R = NHCH2CH2CO2H, Q, Q1, Q2) also seems to be disadvantageous to in vitro activity. In the structure-activity relationship (SAR) study of the 4-substituted quinoline-2-carboxylic acid acid derivs., it was realized that the substitution pattern on C4 significantly influences on the binding affinity for the glycine site of NMDA receptor and the binding affinity might be increased by the introduction of a suitable electron rich substituent at C4 which has the ability of H-bonding donor.

IT **198696-91-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and NMDA receptor antagonist activity of quinolinecarboxylic acid derivs.)

RN 198696-91-2 CAPLUS

CN 2-Quinolinecarboxylic acid, 5,7-dichloro-4-[[(4-methylphenyl)sulfonyl][2-[4-(phenylmethyl)-1-piperazinyl]ethyl]amino]- (9CI) (CA INDEX NAME)




RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

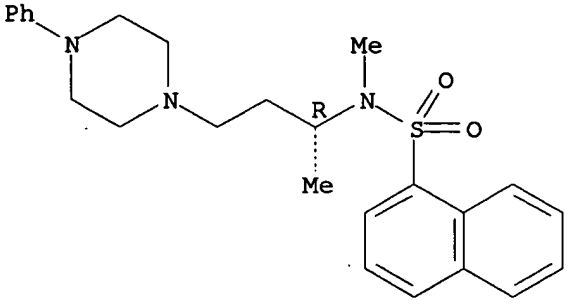
L8 ANSWER 40 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:542438 CAPLUS
DN 127:248014

TI Preparation of piperidinylpropylarenesulfonamide derivatives as 5HT7 receptor antagonists.
IN Forbes, Ian Thomson
PA Smithkline Beecham PLC, UK; Forbes, Ian Thomson
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9729097 | A1 | 19970814 | WO 1997-EP446 | 19970127 |
| | W: JP, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | EP 883613 | A1 | 19981216 | EP 1997-902289 | 19970127 |
| | R: BE, CH, DE, ES, FR, GB, IT, LI, NL | | | | |
| | JP 2000504677 | T2 | 20000418 | JP 1997-528118 | 19970127 |
| PRAI | GB 1996-2679 | A | 19960209 | | |
| | GB 1996-13263 | A | 19960625 | | |
| | WO 1997-EP446 | W | 19970127 | | |

OS MARPAT 127:248014
AB ArSO2NR1(CR2R3)nNR4R5 [Ar = (substituted) mono- or bicyclic (hetero)aryl; R1 = alkyl; R2, R3 = H, alkyl; R4, R5 = H, alkyl, aryl, aralkyl; NR4R5 = (substituted) 5-8 membered heterocyclyl; n = 2-4], were prepd. Thus, 1-methyl-3-(3-methylpiperidin-3-yl)propylamine and Et3N were treated with 1-naphthalenesulfonyl chloride in CH2Cl2 to give 48% N-[1-methyl-3-(3-methylpiperidin-1-yl)propyl]-1-naphthalenesulfonamide. The latter in DMF was treated with NaH and MeI in DMF to give 68% N-methyl-N-[1-methyl-3-(3-methylpiperidin-1-yl)propyl]-1-naphthalenesulfonamide, isolated as the hydrochloride. Title compds. showed pKi = <5.2-7.8 for displacing [3H]-carboxamidotryptamine from 5HT7 receptor clones.
IT **195199-77-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidinylpropylarenesulfonamide derivs. as 5HT7 receptor antagonists)
RN 195199-77-0 CAPLUS
CN 1-Naphthalenesulfonamide, N-methyl-N-[1-methyl-3-(4-phenyl-1-piperazinyl)propyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

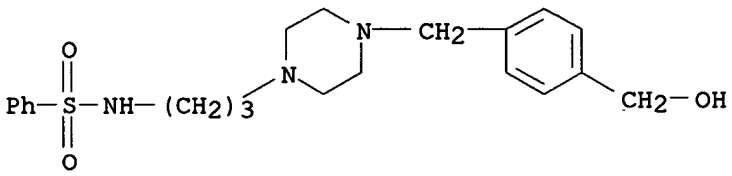



L8 ANSWER 41 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1997:526102 CAPLUS
DN 127:220471
TI Preparation of nitro compounds for treatment of angina pectoris and for prevention of restenosis after percutaneous transluminal coronary angioplasty
IN Uchida, Yasuyoshi; Koga, Hiroshi; Ko, Naoki
PA Chugai Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 30 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 09202764 | A2 | 19970805 | JP 1996-43976 | 19960124 |
| PRAI | JP 1996-43976 | | 19960124 | | |

OS MARPAT 127:220471
AB R1AR2GR3ONO2 [R1 = (un)substituted Ph, naphthyl, anthryl, other arom. hydrocarbyl, (un)substituted pyridyl, quinolyl, isoquinolyl, carbazolyl, indolyl, other heterocyclyl; A = SO2, O, S, (N-substituted) sulfonamido, amido, thioamido, cyanamido; R2 = C1-10 hydrocarbyl; G = SO2, O, S, (N-substituted) sulfonamido, amido, thioamido, cyanamido, amino, cyclic amino; R3 = (un)substituted C1-18 hydrocarbyl (linked via hetero atom)] or their pharmaceutically acceptable salts are prepd. Mesylation of 3.0 g 5-chloro-N-(6-hydroxyhexyl)-1-naphthalenesulfonamide in CH2Cl2 in the presence of 4-dimethylaminopyridine at room temp. for 2.5 h gave 3.54 g 5-chloro-N-(6-methanesulfonyloxyhexyl)-1-naphthalenesulfonamide, which (1.77 g) was treated with 1.01 mL 2-aminoethanol in THF at 70.degree. for 27 h to afford 920 mg 5-chloro-N-[6-(2-hydroxyethylamino)hexyl]-1-naphthalenesulfonamide. The product (200 mg) was treated with urea, fuming HNO3, and Ac2O in CH2Cl2 at room temp. for 4 h to give 60 mg 5-chloro-N-[6-(2-nitroxyethylamino)hexyl]-1-naphthalenesulfonamide nitrate, which at 10-5 M inhibited 52% proliferation of rat vascular smooth muscle cells (A7r5 cells).
IT **195003-63-5P**, N-[3-[4-[4-(Hydroxymethyl)benzyl]piperazin-1-yl]propyl]benzenesulfonamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of antianginal nitro compds.)
RN 195003-63-5 CAPLUS
CN Benzenesulfonamide, N-[3-[4-[[4-(hydroxymethyl)phenyl]methyl]-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)

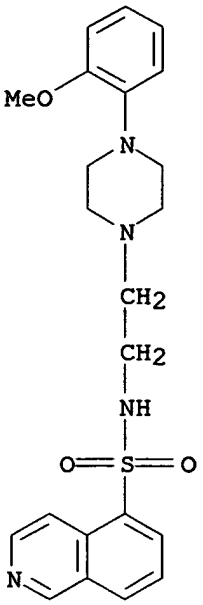


L8 ANSWER 42 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:503173 CAPLUS
DN 127:126664
TI Pharmaceutical compositions containing isoquinolinesulfonyl derivatives for the treatment of glaucoma and ocular ischemia

IN Kapin, Michael A.; Desantis, Louis M., Jr.
PA Alcon Laboratories, Inc., USA; Kapin, Michael A.; Desantis, Louis M., Jr.
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9723222 | A1 | 19970703 | WO 1996-US20197 | 19961220 |
| | W: AU, CA, CN, JP, KR, MX, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | CA 2240271 | AA | 19970703 | CA 1996-2240271 | 19961220 |
| | CA 2240271 | C | 20051213 | | |
| | AU 9714644 | A1 | 19970717 | AU 1997-14644 | 19961220 |
| | AU 720326 | B2 | 20000525 | | |
| | EP 868186 | A1 | 19981007 | EP 1996-945220 | 19961220 |
| | EP 868186 | B1 | 20050302 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | CN 1207680 | A | 19990210 | CN 1996-199673 | 19961220 |
| | JP 2001509780 | T2 | 20010724 | JP 1997-523793 | 19961220 |
| | JP 3719609 | B2 | 20051124 | | |
| | AT 289815 | E | 20050315 | AT 1996-945220 | 19961220 |
| | PT 868186 | T | 20050531 | PT 1996-945220 | 19961220 |
| | ES 2238702 | T3 | 20050901 | ES 1996-945220 | 19961220 |
| | TW 534814 | B | 20030601 | TW 1997-86101346 | 19970204 |
| | US 6271224 | B1 | 20010807 | US 1999-77575 | 19990119 |
| | HK 1015691 | A1 | 20050520 | HK 1999-100710 | 19990227 |
| | US 6403590 | B1 | 20020611 | US 2001-919301 | 20010731 |
| PRAI | US 1995-9351P | P | 19951221 | | |
| | WO 1996-US20197 | W | 19961220 | | |
| | US 1999-77575 | A2 | 19990119 | | |

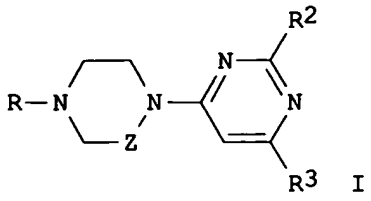
OS MARPAT 127:126664
AB Isoquinolinesulfonyl compds. (Markush structure given) are used in ophthalmic compns. to treat glaucoma or other ischemic-borne ocular disorders such as retinopathies or optic neuropathies. These compds. vasodilate ocular blood vessels, lower intraocular pressure and prevent or reduce the progression of visual field loss. Topical administration of 150.mu.g fasudil hydrochloride (I) to rabbits eyes decreased the intraocular pressure by 14.6% after 1 h. An eye drop contain I 1.5, benzalkonium chloride 0.01, and phosphate buffered saline q.s. 100%.
IT **192712-45-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. isoquinolinesulfonyl derivs. for treatment of glaucoma and ocular ischemia)
RN 192712-45-1 CAPLUS
CN 5-Isoquinolinesulfonamide, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-(9CI) (CA INDEX NAME)



L8 ANSWER 43 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:377861 CAPLUS
DN 126:343579
TI Preparation of pyrimidinylpiperazines as lipid peroxidation inhibitors
IN Toldy, Lajos; Zubovics, Zoltan; Szilagyi, Katalin; Vida, Franciska; Andrasi, Ferenc; Sutka, Klara; Hodula, Eszter; Szekeres, Tibor; Feher, Gabor; Moravcsik, Imre; Matyus, Peter; Sebestyen, Laszlo; Szabo, Hilda; Zara, Erzsebet; Horvath, Edit
PA Gyogyszerkutato Intezet, Hung.; Toldy, Rozsa; Toldy, Marta; Toldy, Andras; Zubovics, Zoltan; Szilagyi, Katalin; Vida, Franciska; Andrasi, Ferenc; Sutka, Klara; et al.
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9714685 | A1 | 19970424 | WO 1996-HU58 | 19961014 |
| | W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA | | | | |
| | HU 76265 | A2 | 19970728 | HU 1995-3012 | 19951019 |
| | AU 9673259 | A1 | 19970507 | AU 1996-73259 | 19961014 |
| PRAI | HU 1995-3012 | A | 19951019 | | |
| | WO 1996-HU58 | W | 19961014 | | |

OS MARPAT 126:343579
GI



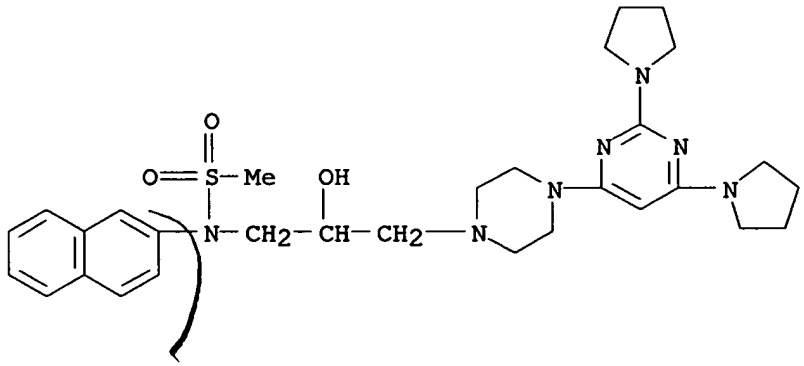
I

AB Title compds. [I; R = AX(CH2)r(CO)q(CH2)pR1; A = (un)substituted alkylene; R1 = (un)substituted aryl; R2,R3 = NH2 or N-attached heterocyclyl; X = bond, SO0-2, (un)substituted imino; Z = CH2 or CH2CH2; p,q,r = 0 or 1] were prepd. Thus, 1-[2-hydroxy-3-(2-naphthylthio)propyl]piperazine (prepn. given) was N-arylated by 2,6-diamino-4-chloropyrimidine to give I [R = R1SCH2CH(OH)CH2, R1 = 2-naphthyl, R2 = R3 = NH2, Z = CH2]. Data for biol. activity of I were given.

IT **190000-58-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrimidinylpiperazines as lipid peroxidn. inhibitors)

RN 190000-58-9 CAPLUS

CN Methanesulfonamide, N-[3-[4-(2,6-di-1-pyrrolidinyl-4-pyrimidinyl)-1-piperazinyl]-2-hydroxypropyl]-N-2-naphthalenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 44 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1997:305811 CAPLUS

DN 127:16456

TI The isoquinoline derivative KN-62 a potent antagonist of the P2Z-receptor of human lymphocytes

AU Gargett, Caroline E.; Wiley, James S.

CS Department of Haematology, Austin and Repatriation Medical Centre, Heidelberg, VIC 3084, Australia

SO British Journal of Pharmacology (1997), 120(8), 1483-1490
CODEN: BJPCBM; ISSN: 0007-1188

PB Stockton

DT Journal

LA English

AB Extracellular ATP is an agonist for a P2Z receptor on human lymphocytes which mediates opening of a cation-selective ion channel, activation of phospholipase D, and shedding of the adhesion mol., L-selectin, from the

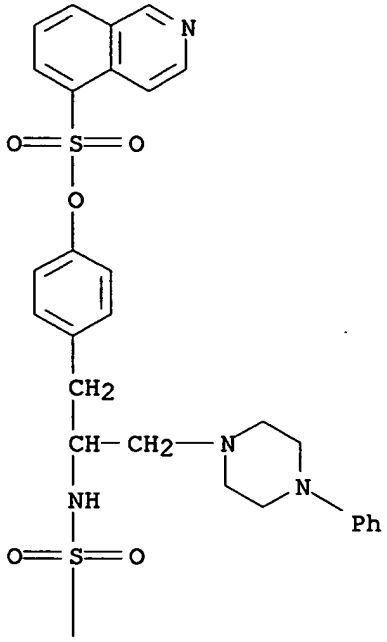
cell surface. The isoquinolinesulfonamides, KN-62, (1-[N, O-bis(5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phenylpiperazine), a selective antagonist of Ca2+/calmodulin-dependent protein kinase II (CaMKII), and KN-04, (N-[1-[N-methyl-p-(5 isoquinoline sulfonyl)benzyl]-2-(4 phenylpiperazine)ethyl]-5-isoquinolinesulfonamide) an inactive analog, were used to investigate the possible role of CaMKII in these diverse effects of extracellular ATP. KN-62 potently antagonized ATP-stimulated Ba2+ influx into fura-2 loaded human lymphocytes with an IC50 of 12.7 nM and complete inhibition of the flux at a concn. of 500 nM. Similarly, KN-62 inhibited ATP-stimulated ethidium+ uptake, measured by time resolved flow cytometry, with an IC50 of 13.1 nM and complete inhibition of the flux at 500 nM. KN-04 antagonized ATP-stimulated Ba2+ influx with an IC50 of 17.3 nM. Similarly, KN-04 inhibited ATP-stimulated ethidium+ uptake with an IC50 of 37.2 nM. Both fluxes were completely inhibited at 500 nM KN-04. ATP-stimulated phospholipase D activity, measured in [3H]-oleic acid-labeled lymphocytes by the transphosphatidylation reaction, was antagonized by KN-62 and KN-04, with 50% inhibition at 5.9 and 9.7 nM, resp. Both KN-62 and KN-04 inhibited ATP-stimulated shedding of L-selectin, measured by flow cytometric anal. of cell surface L-selectin, with IC50 values of 31.5 and 78.7 nM, resp. Neither of the isoquinolinesulfonamides (500 nM) inhibited phorbol ester- or ionomycin-stimulated phospholipase D activity or phorbol ester-induced shedding of L-selectin. The inhibitory effect of KN-62 or KN-04 on P2Z-mediated responses was slow in onset (5 min) and only partially reversed by washing the cells. Both KN-62 and KN-04 (at 500 nM) had no effect on UTP-stimulated Ca2+ transients in fura-2 loaded human neutrophils, a response which is mediated by the P2Y2 receptor. Thus, KN-62 and KN-04 are potent antagonists of the P2Z receptor and at nanomolar concns. inhibit all known responses mediated by the P2Z receptor of human lymphocytes. In contrast, KN-62 and KN-04 had no effect on responses mediated by the P2Y2 receptor of neutrophils. Moreover, since KN-62 and KN-04 are almost equipotent, the P2Z-mediated responses do not involve CaMKII, but indicate that the isoquinolinesulfonamides are potent and direct inhibitors of the P2Z-receptor.

IT **129695-80-3**, KN-04
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(isoquinoline deriv. KN-62 and its inactive analog as antagonists of P2Z-receptor of human lymphocytes)

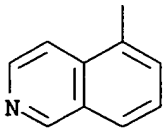
RN 129695-80-3 CAPLUS

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

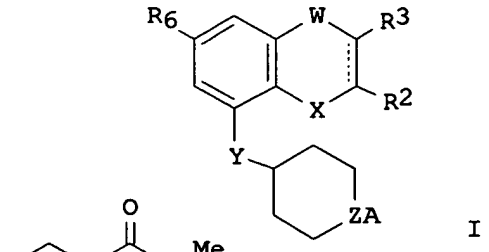
L8 ANSWER 45 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:169157 CAPLUS
DN 126:225315
TI Bicyclic heterocyclic derivatives having .alpha.1-adrenergic and 5HT1A serotonergic activities
IN Leonardi, Amedeo; Motta, Gianni; Riva, Carlo; Testa, Rodolfo
PA Recordati S.A., Chemical and Pharmaceutical Company, Switz.
SO U.S., 84 pp., Cont.-in-part of U.S. 5,474,994.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5605896 | A | 19970225 | US 1994-299188 | 19940831 |
| | US 5403842 | A | 19950404 | US 1992-888775 | 19920526 |
| | AU 9336296 | A1 | 19930913 | AU 1993-36296 | 19930223 |

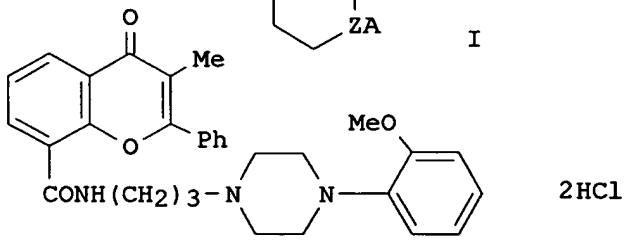
| | | | | | |
|---|---|---|---|---|---|
| | RO 112111 | B3 | 19970530 | RO 1994-1404 | 19930223 |
| | PL 175556 | B1 | 19990129 | PL 1993-304889 | 19930223 |
| | RU 2128656 | C1 | 19990410 | RU 1994-43324 | 19930223 |
| | SK 280143 | B6 | 19990910 | SK 1994-1007 | 19930223 |
| | ZA 9301278 | A | 19931118 | ZA 1993-1278 | 19930224 |
| | LT 3038 | B | 19940925 | LT 1993-354 | 19930224 |
| | CN 1079738 | A | 19931222 | CN 1993-105852 | 19930526 |
| | CN 1040434 | B | 19981028 | | |
| | US 5474994 | A | 19951212 | US 1993-67861 | 19930526 |
| | FI 9403876 | A | 19940823 | FI 1994-3876 | 19940823 |
| | NO 9403140 | A | 19940825 | NO 1994-3140 | 19940825 |
| PRAI | IT 1992-MI408 | A | 19920225 | | |
| | US 1992-888775 | A2 | 19920526 | | |
| | US 1993-67861 | A2 | 19930526 | | |
| | EP 1993-301264 | A | 19930222 | | |
| | WO 1993-EP420 | A | 19930223 | | |

OS MARPAT 126:225315

GI

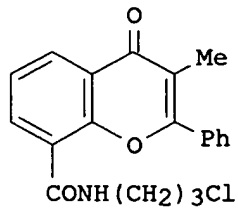



I




2HCl

II




III

AB Bicyclic heterocyclic derivs., such as I [X = N, O, S; W = C(O), C(S), CH(OH), bond; R2 = H, optionally substituted alkyl, alkenyl, alkylnyl, carbocycle, heterocycle; R3 = alkyl, hydroxyalkyl, Ph, OH, alkoxy, alkoxyalkyl; R6 = H, halogen, NO2, NH2, AcNH, mono-, dialkylamino, CN, OH, alkoxy, alkyl; Y = CO, CO2, CONH, CH(OH), CH:CH, CH:CHCO2, CH:CHCONH, CH2NH, CH2NHCO, CH2NHSO2, CH2O, CH2S, NH, NHCO, NHCONH, NHSO2, O, S, SO2NH, CONHO, CSNH, NHCO2, COS, CONH(CH2)m, m = 1-6; Z = N, A = (un)substituted Ph, pyrimidinyl, 1,4-benzodioxan-8-yl, benzopyran-8-yl, benzofuran-7-yl, dihydrobenzopyran-8-yl; Z = CH2N; Z = CH, A = one or two

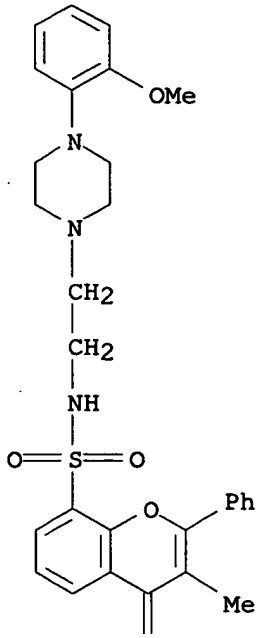
Ph, 4-FC6H4CO, 2-oxo-1-benzimidazolinyl, (CH2)nOA, n = 0-2], and their pharmaceutically acceptable salts useful as .alpha.1-adrenergic and 5HT1A serotonergic agents for the treatment of hypertension, urethral and lower urinary tract contractions, and other disorders are described. Thus, benzopyran II was prepd. by heating 1-(2-methoxyphenyl)piperazine with benzopyran III at 180.degree. for 5 h. II had IC50 = 29 nM for .alpha.1-adrenergic receptor binding, IC50 = 9 nM for 5HT1A receptor binding, ED25 = 45 .mu.g/kg i.v. hypotensive effect and ED25 = 1.4 .mu.g/kg in Na-induced urethral contractility assays.

IT **152735-59-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bicyclic heterocyclic derivs. having .alpha.1-adrenergic and 5HT1A serotonergic activities)

RN 152735-59-6 CAPLUS

CN 4H-1-Benzopyran-8-sulfonamide, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-methyl-4-oxo-2-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



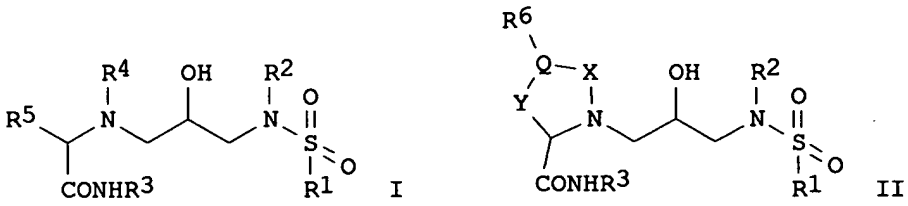

PAGE 2-A


● HCl

L8 ANSWER 46 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:563465 CAPLUS
DN 125:195206
TI Preparation of N-(2-hydroxy-3-aminopropyl)sulfonamides
IN Sprengeler, Paul; Smith, Amos B., III; Hirschmann, Ralph F.; Yokoyama, Akihisa
PA Trustees of the University of Pennsylvania, USA
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9622097 | A1 | 19960725 | WO 1996-US576 | 19960116 |
| W: CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5612339 | A | 19970318 | US 1995-373651 | 19950117 |
| PRAI US 1995-373651 | A | 19950117 | | |

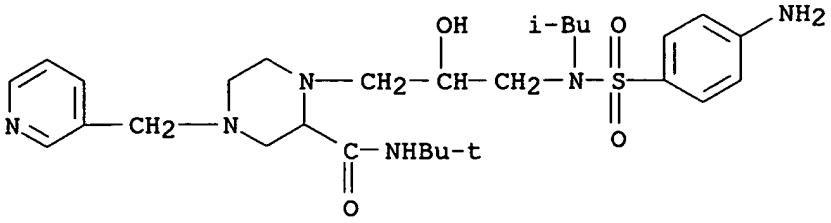
OS MARPAT 125:195206
GI



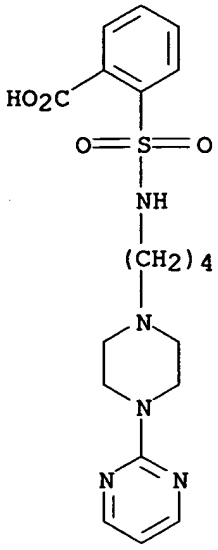
AB The title compds. [I and II, R1 = H, OH, C1-10 alkyl, C3-20 aryl; R2, R4, R6 = H, C1-10 alkyl, C3-20 aryl, etc.; R3 = H, C1-10 alkyl, C4-25 alkaryl; R5 = H, C1-10 alkyl, C3-20 aryl; X, Y = C1-6 alkylene; Q = N, CH2], useful as antibacterial agents (no data), were claimed. Synthesis of compd. I [R1 = 4-N2NC6H4; R2 = iBu; R3 = tBu; Q = N; X = (CH2)2; Y = CH2; R6 = 3-pyridylmethyl] is described.

IT **178942-68-2P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-(2-hydroxy-3-aminopropyl)sulfonamides)

RN 178942-68-2 CAPLUS
CN 2-Piperazinecarboxamide, 1-[3-[[(4-aminophenyl)sulfonyl](2-methylpropyl)amino]-2-hydroxypropyl]-N-(1,1-dimethylethyl)-4-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



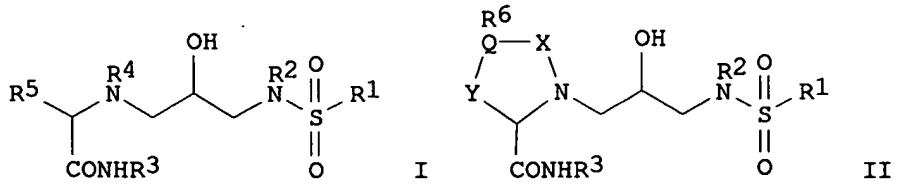
L8 ANSWER 47 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:407459 CAPLUS
DN 125:96333
TI Assay and purity control of new serotonergic anxiolytics by HPTLC and scanning densitometry
AU Farina, Anna; Doldo, Antonio; Cotichini, Viviana; Rajevic, Maya
CS Lab. Chimica Farmaco, Ist. Sup. Sanita, Rome, 00161, Italy
SO Journal of Planar Chromatography--Modern TLC (1996), 9(3), 185-188
CODEN: JPCTE5; ISSN: 0933-4173
PB Research Institute for Medicinal Plants
DT Journal
LA English
AB A high-performance TLC (HPTLC) method with densitometric UV detection was used for the detn. and purity control of serotonergic anxiolytics. With silica gel as adsorbent and 3 different mobile phases, all the potential impurities were well sepd. from the main components and from each other. Detection limits of a few nanograms were obtained at a signal-to-noise ratio 3:1. The relative std. deviation values for the main components and related impurities were between 2.2 and 3.4%. The results obtained were compared with those obtained by a previously established HPLC method.
IT **164030-31-3**
RL: ANT (Analyte); ANST (Analytical study)
(purity control of serotonergic anxiolytics by HPTLC and densitometry)
RN 164030-31-3 CAPLUS
CN Benzoic acid, 2-[[[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]amino]sulfonyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 48 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:366115 CAPLUS
DN 125:115158
TI Peptidomimetic N-(2-hydroxy-3-aminopropyl)sulfonamides as proteolytic enzyme inhibitors
IN Sprengeler, Paul; Smith, Amos B., III; Hirschmann, Ralph F.; Yokoyama, Akihisa
PA University of Pennsylvania, USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 5519060 | A | 19960521 | US 1995-373564 | 19950117 |
| WO 9622087 | A1 | 19960725 | WO 1996-US501 | 19960116 |
| W: CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| PRAI US 1995-373564 | A | 19950117 | | |

OS MARPAT 125:115158
GI



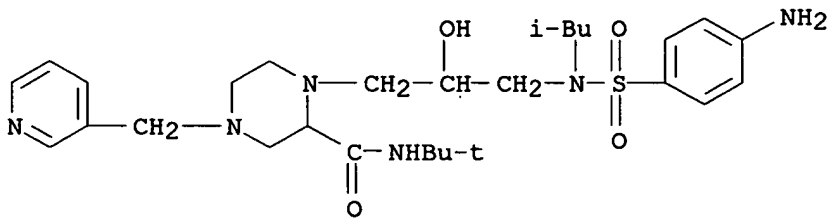
AB A method is claimed for modulating the activity of an enzyme (no data), comprising contacting said enzyme with at least one compd. having

structure I or II: wherein: R1 is H, OH, alkyl having 1 to about 10 carbon atoms, or aryl having 3 to about 20 carbon atoms; R2 is H, alkyl having 1 to about 10 carbon atoms, aryl having 3 to about 20 carbon atoms, alkaryl having 4 to about 25 carbon atoms, or an amino acid side chain; R3 is H, alkyl having one to about 10 carbon atoms, or alkaryl having 4 to about 25 carbon atoms; R4 is H, alkyl having 1 to about 10 carbon atoms, aryl having 3 to about 20 carbon atoms, alkaryl having 4 to about 25 carbon atoms, or an amino acid side chain; R5 is H, alkyl having one to about 10 carbon atoms, or aryl having 3 to about 20 carbon atoms; R6 is H, alkyl having one to about 10 carbon atoms, aryl having 3 to about 20 carbon atoms, or alkaryl having 4 to about 25 carbon atoms; X and Y are, independently, alkylene having 1 to about 6 carbon atoms, provided that the sum of X and Y is less than or equal to 9; and Q is N or CH2. Synthetic schemes for the prepn. of representative II structures are provided.

IT **178942-68-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidomimetic N-(2-hydroxy-3-aminopropyl)sulfonamides as proteolytic enzyme inhibitors)

RN 178942-68-2 CAPLUS

CN 2-Piperazinecarboxamide, 1-[3-[[(4-aminophenyl)sulfonyl](2-methylpropyl)amino]-2-hydroxypropyl]-N-(1,1-dimethylethyl)-4-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)




L8 ANSWER 49 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1996:234316 CAPLUS

DN 124:338800

TI The Ca2+/calmodulin-dependent protein kinase II inhibitors KN62 and KN93, and their inactive analogs KN04 and KN92, inhibit nicotinic activation of tyrosine hydroxylase in bovine chromaffin cells

AU Marley, Philip D.; Thomson, Kerrie A.

CS Dep. Pharmacol., Univ. Melbourne, Parkville, 3052, Australia

SO Biochemical and Biophysical Research Communications (1996), 221(1), 15-18
CODEN: BBRCA9; ISSN: 0006-291X

PB Academic

DT Journal

LA English

AB The possible role of Ca++/calmodulin-dependent protein kinase II (CAM-K-II) in the nicotinic activation of tyrosine hydroxylase in intact cultured bovine adrenal chromaffin cells was investigated. Over the concn. range 3-30 .mu.M, KN62, a specific CAM-K-II inhibitor, inhibited basal tyrosine hydroxylase activity and the activity stimulated by nicotine or K+ depolarization. KN04, a structural analog of KN62 which does not inhibit CAM-K-II, produced an identical concn.-dependent

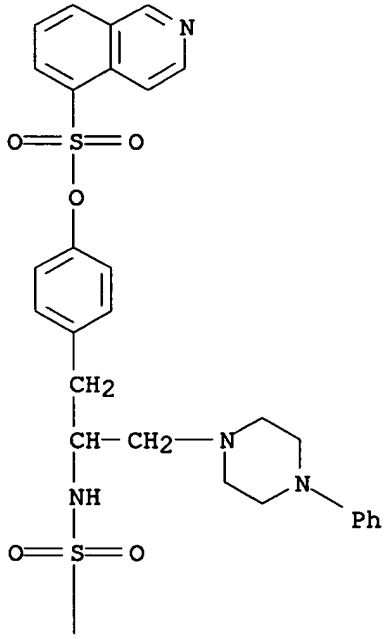
inhibition of basal and nicotine-stimulated tyrosine hydroxylase activity. Another CAM-K-II inhibitor, KN93, also inhibited nicotine and K+ stimulation of tyrosine hydroxylase activity; however, an inactive analog of KN93, KN92, mimicked these effect. The results suggest that the inhibition of nicotine- and K+-stimulated tyrosine hydroxylase activity by KN62 and KN93 is not due to their ability to inhibit CAM-K-II.

IT **129695-80-3**, KN04
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Ca2+/calmodulin-dependent protein kinase II inhibitors KN62 and KN93, and their inactive analogs KN04 and KN92, inhibit nicotinic activation of tyrosine hydroxylase in bovine chromaffin cells)

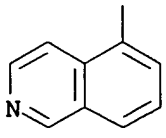
RN 129695-80-3 CAPLUS

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L8 ANSWER 50 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:157139 CAPLUS
DN 124:256714

TI KN-62, a calcium/calmodulin-dependent protein kinase II inhibitor, inhibits high potassium-stimulated prolactin secretion and intracellular calcium increases in anterior pituitary cells

AU Cui, Z. J.; Hidaka, H.; Dannies, P. S.
CS Department of Pharmacology, Yale University School of Medicine, 333 Cedar Street, New Haven, CT, 06510, USA

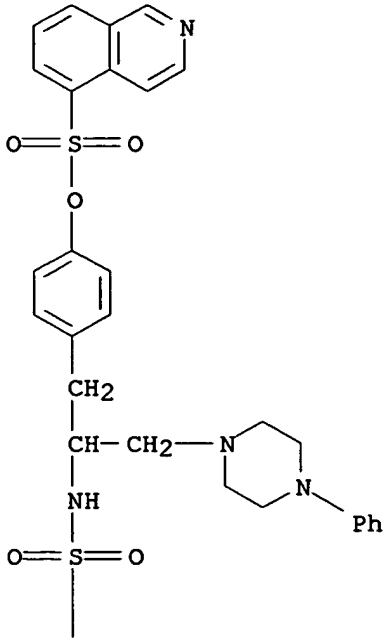
SO Biochimica et Biophysica Acta, Molecular Cell Research (1996), 1310(3), 343-7
CODEN: BBAMCO; ISSN: 0167-4889
PB Elsevier B.V.
DT Journal
LA English

AB In isolated rat anterior pituitary cells, KN-62 (10 .mu.M), an isoquinoline sulfonamide inhibitor of calcium/calmodulin-dependent protein kinase II, inhibited high KCl(50 mM)-stimulated prolactin secretion almost completely, with an IC50 of 95 nM. KN-62 inhibited TRH-induced prolactin secretion less effectively. KN-04, a compd. that is over 100-fold less active in inhibiting purified calcium/calmodulin-dependent protein kinase II, also inhibited high KCl-stimulated prolactin secretion with an IC50 of 500 nM. KN-62 and KN-04 (10 .mu.M) both inhibited high KCl-stimulated increases in intracellular Ca2+ concns. The authors conclude that KN-62 and KN-04 inhibit activation of voltage-dependent calcium channels in anterior pituitary cells either directly or indirectly.

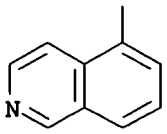
IT **129695-80-3**, KN-04
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(KN-62, a calcium/calmodulin-dependent protein kinase II inhibitor, inhibits high potassium-stimulated prolactin secretion and intracellular calcium increases in anterior pituitary cells)

RN 129695-80-3 CAPLUS
CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

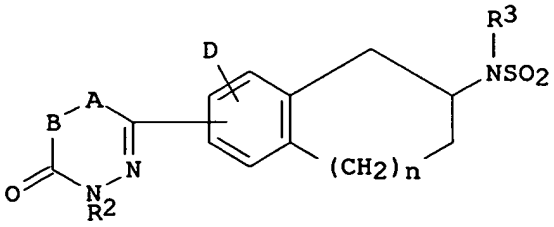


L8 ANSWER 51 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:52662 CAPLUS
DN 124:176127
TI Preparation of sulfamoylindanyl- and sulfamoyl-1,2,3,4-tetrahydronaphthylpyridazinone derivatives as drugs
IN Ishida, Akihiko; Pponma, Koichi; Kono, Haruyuki; Tamura, Koji; Sasaki, Yasuhiko
PA Tanabe Seiyaku Co, Japan
SO Jpn. Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 07233072 | A2 | 19950905 | JP 1994-322942 | 19941226 |
| PRAI | JP 1994-322942 | A | 19941226 | | |
| | JP 1993-333966 | | 19931228 | | |

OS MARPAT 124:176127

GI



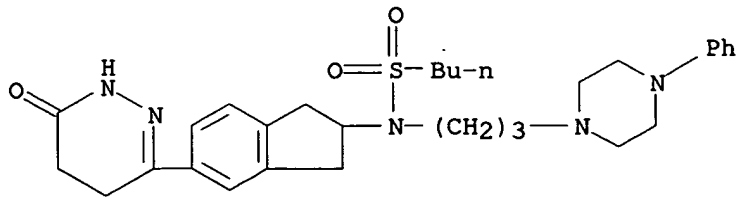
I

AB The title compds. [I; R1 = (un)substituted C1-10 alkyl, C3-6 cycloalkyl, lower alkenyl, (un)substituted heterocyclyl contg. N, O, or S heteroatom, camphor-10-yl; R3 = H, (un)substituted lower alkyl, lower alkenyl; or R1 and R3 are linked to each other at the termini to form a lower alkylene; R2 = H, (un)substituted lower alkyl, aryl, lower alkenyl; A-B = ethylene or vinylene optionally substituted by 1-2 groups selected from lower alkyl or Ph; n = 1,2; D = H, halo], which are useful for the treatment and prevention of nephritis, in particular glomerulonephritis, IgA nephritis, nephrotic syndrome, and/or lupus nephritis and as blood platelet aggregation inhibitors and/or protective agents against endotoxin shock, are prepd. Thus, 1.15 g 2-amino-5-[3-oxo-3(H)-4,5-dihydropyridazin-6-yl]indan was dissolved in EtOAc and THF, followed by successively adding an aq. soln. of 1.4 g K2CO3 in 20 mL and 0.57 g MeSO2Cl, and the resulting mixt. was stirred for 2 h to give 1.08 g 2-methanesulfonylamino-5-[3-oxo-3(H)-4,5-dihydropyridazin-6-yl]indan (II). Mice was administered with II at 100 mg/kg p.o. and after 30 min treated with a soln. of Escherichia coli-derived endotoxin (lipopolysaccharides) in physiol. saline at 100 mg/10 mL/kg i.p. The survival ratio of the treated mice was 100 %.

IT **172680-06-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfamoylindanyl- and sulfamoyltetrahydronaphthylpyridazinone derivs. as drugs)

RN 172680-06-7 CAPLUS

CN 1-Butanesulfonamide, N-[2,3-dihydro-5-(1,4,5,6-tetrahydro-6-oxo-3-pyridazinyl)-1H-inden-2-yl]-N-[3-(4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



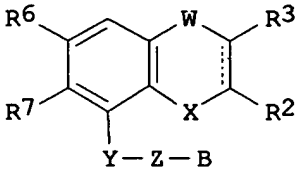
L8 ANSWER 52 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1996:35000 CAPLUS

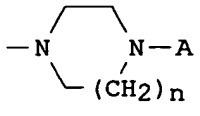
DN 124:232248
TI Benzopyran derivatives having affinity for .alpha.1-adrenergic and 5HT1A-serotoninergic receptors
IN Leonardi, Amedeo; Motta, Gianni; Riva, Carlo; Testa, Rodolfo
PA Recordati S.A., Chemical and Pharmaceutical Company, Switz.
SO U.S., 37 pp. Cont.-in-part of U.S. 5,403,842.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5474994 | A | 19951212 | US 1993-67861 | 19930526 |
| | US 5403842 | A | 19950404 | US 1992-888775 | 19920526 |
| | EP 558245 | A1 | 19930901 | EP 1993-301264 | 19930222 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | AU 9336296 | A1 | 19930913 | AU 1993-36296 | 19930223 |
| | RO 112111 | B3 | 19970530 | RO 1994-1404 | 19930223 |
| | PL 175556 | B1 | 19990129 | PL 1993-304889 | 19930223 |
| | SK 280143 | B6 | 19990910 | SK 1994-1007 | 19930223 |
| | CN 1079738 | A | 19931222 | CN 1993-105852 | 19930526 |
| | CN 1040434 | B | 19981028 | | |
| | FI 9403876 | A | 19940823 | FI 1994-3876 | 19940823 |
| | NO 9403140 | A | 19940825 | NO 1994-3140 | 19940825 |
| | US 5605896 | A | 19970225 | US 1994-299188 | 19940831 |
| PRAI | US 1992-888775 | A2 | 19920526 | | |
| | EP 1993-301264 | A | 19930222 | | |
| | IT 1992-MI408 | A | 19920225 | | |
| | WO 1993-EP420 | A | 19930223 | | |
| | US 1993-67861 | A2 | 19930526 | | |

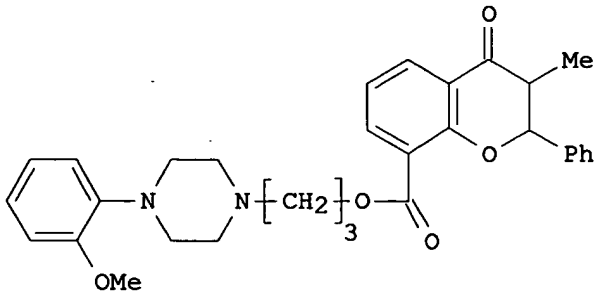
OS MARPAT 124:232248
GI




I




II




III

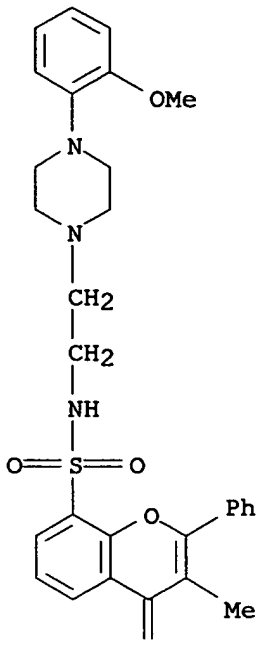
AB This invention provides bicyclic heterocyclic derivs. I wherein the dotted line represents a single or double bond; X represents a nitrogen, oxygen or sulfur atom, or an amino or alkylamino group, a sulfinyl or sulfonyl group; W represents a carbonyl, thiocarbonyl, hydroxymethylene, or a methylene group or a bond; or when X is nitrogen and W is a methine, the fused rings represent a quinoline; R2 represents, e.g, a hydrogen atom or an alkyl, alkenyl, alkynyl, carbocyclic or heterocyclic group, each of which groups may optionally be substituted; or R2 itself represents a trifluoromethyl or an aroyl group; R3 represents a hydrogen atom or an alkyl, hydroxyalkyl, alkyl-O-R4 Ph, hydroxy, or O-R4, wherein R4 represents an alkyl group optionally substituted with an aryl group; R6 represents a hydrogen or halogen atom or a nitro, amino, acylamino, alkylsulfonylamino, alkylamino, dialkylamino, cyano, hydroxy, alkoxy or alkyl group; R7 represents a hydrogen atom or an alkoxy group; Y = e.g., CO, COO, CONH; Z represents a linear or branched chain alkylene group having from 1 to 6 carbon atoms and optionally having one hydroxy substituent; B = e.g., II, n = 1 or 2, A = substituted Ph, 2-pyrimidinyl; and their pharmaceutically acceptable salts useful for the treatment of hypertension, urethral and lower urinary tract contractions, and other disorders. The compds. are also useful for binding .alpha.1-adrenergic and 5HT1A serotonergic receptors, in vitro or in vivo. Thus, e.g., esterification of 8-carboxy-3-methyl-4-oxo-2-phenyl-4H-1-benzopyran with 1-(3-chloropropyl)-4-(2-methoxyphenyl)piperazine followed by HCl treatment afforded 8-{3-[4-(2-methoxyphenyl)-1-piperazinyl]propoxycarbonyl}-3-methyl-4-oxo-2-phenyl-4H-1-benzopyran dihydrochloride (III.2HCl) which exhibited IC50's of 20 and 19 nM, resp., for .alpha.1 and 5-HT1A receptor binding. Data were also presented for the effect of I on K+ stimulation of rat bladder strips, and on urethral contractions and blood pressure in dogs.

IT **152735-59-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzopyran derivs. having affinity for .alpha.1-adrenergic and 5HT1A-serotoninergic receptors)

RN 152735-59-6 CAPLUS

CN 4H-1-Benzopyran-8-sulfonamide, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-methyl-4-oxo-2-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



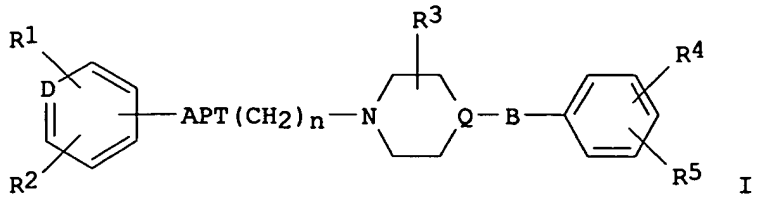

PAGE 2-A


● HCl

L8 ANSWER 53 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:902630 CAPLUS
DN 123:313770
TI Preparation of piperidino and piperazino 5-HT2 receptor antagonists and blood platelet aggregation inhibitors
IN Aoki, Tsuyoshi; Takahashi, Atsuo; Sato, Hiroyasu; Shimanuki, Eiji; Gengyou, Kaoru; Nishimata, Toyoki; Ishigami, Sachiko; Yamada, Shin-ichi; Yamaguchi, Takahiro; et al.
PA Toa Eiyo Ltd., Japan
SO Eur. Pat. Appl., 123 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 661266 | A1 | 19950705 | EP 1994-120698 | 19941227 |
| | R: BE, CH, DE, ES, FR, GB, IT, LI, LU, NL | | | | |

JP 07242629 A2 19950919 JP 1994-336707 19941226
PRAI JP 1993-346805 A 19931227
OS MARPAT 123:313770
GI



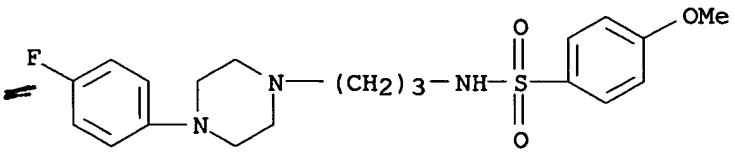
I

AB The title compds. [I; A = CH2, CO, sulfonyl; B, T = direct bond, CH2, CO, CH(OH), C(:NH); D = CH, N, N.fwdarw.O; P = N, N.fwdarw.O; Q = CH, N; R1, R2 = H, OH, (un)branched alkyl, alkenyl, (un)substituted aralkyl, acyl, (un)substituted NH2, etc.; R3 = H, OH, (un)branched alkyl or alkoxy; R4, R5 = H, OH, halogen, (un)branched alkyl, alkenyl, alkoxy, alkylthio, (un)substituted NH2, SH, etc.; n = 1-6], useful as 5-HT2 receptor antagonists and blood platelet aggregation inhibitors, are prepd. Thus, 4-acetylamino-N-[2-[4-(4-fluorobenzoyl)piperidino]ethyl]-N-(3-methoxyphenyl)benzamide fumarate, m.p. 215-222.degree. (decompn.), prepd. by the reaction of the free base with fumaric acid, demonstrated a IC50 for platelet aggregation in rabbit-derived, platelet-rich plasma of .ltoreq.9.9 x 10-8 M, vs. 1.0-9.9 x 10-7 M for ketanserin.

IT **169945-97-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidino and piperazino 5-HT2 receptor antagonists and blood platelet aggregation inhibitors)

RN 169945-97-5 CAPLUS

CN Benzenesulfonamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-4-methoxy- (9CI) (CA INDEX NAME)



L8 ANSWER 54 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1995:807948 CAPLUS

DN 123:228215

TI Piperazine derivatives as .alpha.1A-adrenergic receptor antagonists

IN Leonardi, Amedeo; Motta, Gianni; Riva, Carlo; Testa, Rodolfo

PA Recordati Industria Chimica e Farmaceutica S.p.A, Italy; Recordati S.A., Chemical and Pharmaceutical Co.

SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2

DT Patent

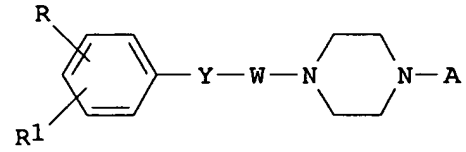
LA English

FAN.CNT 1

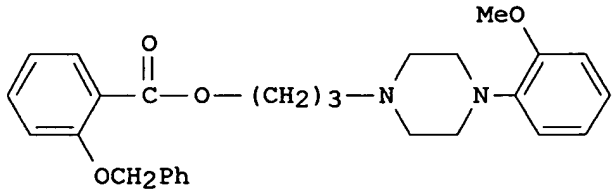
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9504049 | A1 | 19950209 | WO 1994-EP2437 | 19940722 |
| | W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN | | | | |
| | RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2168443 | AA | 19950209 | CA 1994-2168443 | 19940722 |
| | AU 9475323 | A1 | 19950228 | AU 1994-75323 | 19940722 |
| | AU 680037 | B2 | 19970717 | | |
| | EP 711288 | A1 | 19960515 | EP 1994-925382 | 19940722 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | CN 1132508 | A | 19961002 | CN 1994-193622 | 19940722 |
| | JP 09500883 | T2 | 19970128 | JP 1994-505546 | 19940722 |
| | ZA 9405625 | A | 19950307 | ZA 1994-5625 | 19940729 |
| | NO 9600371 | A | 19960329 | NO 1996-371 | 19960129 |
| PRAI | IT 1993-MI1717 | A | 19930730 | | |
| | WO 1994-EP2437 | W | 19940722 | | |

OS CASREACT 123:228215; MARPAT 123:228215

GI




I




II

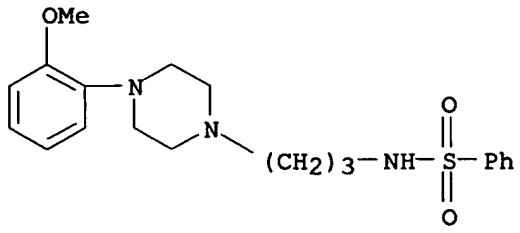
AB Title compds. I are disclosed [in which Y = bond, SOn, NR2, NR2CO, PO(OEt)NH, NHCONH, CO, SO2NR2, (CH2)nCOO, (CH2)nCONR2; W = C2-6 alkylene; A = substituted Ph, or a benzofuran or benzodioxan group; R and R1 have many values, but R is preferably bulky; with provisos]. I and their prodrugs, enantiomers, diastereoisomers, N-oxides, and pharmaceutically acceptable salts block .alpha.1A-adrenergic receptors, and are useful for preventing contractions of the prostate, urethra and lower urinary tract, without affecting blood pressure. Because of their generally low toxicity, less selective I at higher dosages may also be useful as antihypertensives. For example, O-alkylation of 2-benzyloxybenzoic acid with 1-(3-chloropropyl)-4-(2-methoxyphenyl)piperazine in DMF in the presence of K2CO3 at 80.degree. gave title compd. II, isolated as its di-HCl salt (III). Compared to prazosin (IV), III had slightly lower .alpha.1A-adrenoceptor affinity and comparable oral toxicity in mice, but in expts. on urethral contractility and blood pressure in dogs, III showed higher selectivity for urethral activity, with a blood pressure/urethral ED ratio of 6.7, vs. 1.8 for IV and 2.6 for urapidil.

IT **168053-03-0P**

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazine derivs. as .alpha.1A-adrenergic receptor antagonists)

RN 168053-03-0 CAPLUS

CN Benzenesulfonamide, N-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)




L8 ANSWER 55 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1995:537305 CAPLUS

DN 123:18065

TI Analysis of non-benzodiazepinic anxiolytic agents by capillary zone electrophoresis

AU Quaglia, M. G.; Farina, A.; Boxxu, E.; Dell'aquila, C.

CS Dip. Farm., Univ. "La Sapienza", Rome, 00185, Italy

SO Journal of Pharmaceutical and Biomedical Analysis (1995), 13(4/5), 505-9
CODEN: JPBADA; ISSN: 0731-7085

PB Elsevier

DT Journal

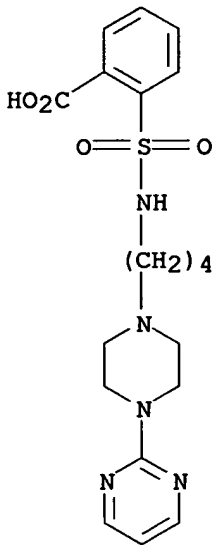
LA English

AB A simple capillary electrophoretic method was developed for the anal. of a new generation of and their related substances: zalospirone, gepirone, ipsapirone and busipirone. All compds. run in a Tris/phosphate buffer at pH 3 as cations and the exptl. conditions allowed good resoln. of four drugs and their principal impurities. The anal. were made using two different kinds of capillary. The suitability of CZE and HPLC methods for the anal. of these non-benzodiazepinic anxiolytic agents and their impurities was compared.

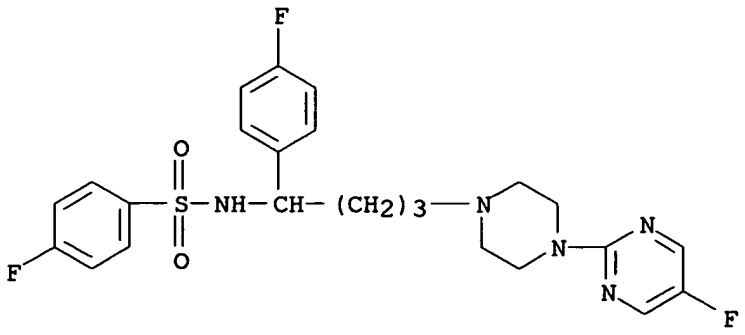
IT **164030-31-3**
RL: ANT (Analyte); ANST (Analytical study)
(serotonergic anxiolytics detn. by capillary zone electrophoresis)

RN 164030-31-3 CAPLUS

CN Benzoic acid, 2-[[[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]amino]sulfonyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 56 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:63852 CAPLUS
DN 122:71338
TI Synthesis and evaluation of N-substituted 1-(5-fluoro-2-pyrimidinyl)piperazine derivatives as potential anti-ischemic agents
AU Yevich, Joseph P.; Dextraze, Pierre; Taylor, Duncan P.; Moon, Sandra L.
CS Bristol-Myers Squibb Pharm. Res. Inst., Wallingford, CT, 06492-7660, USA
SO Bioorganic & Medicinal Chemistry Letters (1994), 16(4), 1941-6
CODEN: BMCLE8; ISSN: 0960-894X
DT Journal
LA English
AB A no. of N-substituted 1-(5-fluoro-2-pyrimidinyl)piperazine derivs. were prepd. and evaluated for binding to sigma and serotonin 5-HT1A and 5-HT2 receptor subtypes as well as for their protection against nitrogen anoxia-induced lethality in rats. Although various compds. exhibited good binding affinity and/or anti-anoxic effects, there was no obvious correlation between their receptor binding and in vivo effects. Structure-activity relations are examd.
IT **133982-23-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis and evaluation of N-substituted (fluoropyrimidinyl)piperazine derivs. as potential anti-ischemic agents in relation to receptor binding)
RN 133982-23-7 CAPLUS
CN Benzenesulfonamide, 4-fluoro-N-[1-(4-fluorophenyl)-4-[4-(5-fluoro-2-pyrimidinyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 57 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:557540 CAPLUS
DN 121:157540
TI 5-Isoquinolinesulfonamide derivatives
IN Kabashima, Shigeru; Nagumo, Hiromitsu
PA Asahi Chemical Ind, Japan
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 06100540 | A2 | 19940412 | JP 1992-254605 | 19920924 |
| PRAI | JP 1992-254605 | | 19920924 | | |

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

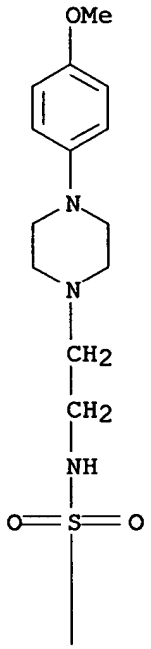
AB Title derivs. I [R1 = NHCH2CH2R2, NHCH2CHMeNH(CH2)5Me, Q, Q1; R2 = Q2-10] and their salts with acids, useful as inhibitors of protein kinase, are prepd. Thus, stirring a mixt. of 5-isoquinolinesulfonyl chloride, (2-aminoethyl)morpholine, and Et3N in CH2Cl2 at room temp. gave 71% 5-(2-morpholinoethylaminosulfonyl)isoquinoline.

IT **157383-17-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for protein kinase inhibitor)

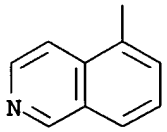
RN 157383-17-0 CAPLUS

CN 5-Isoquinolinesulfonamide, N-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



● HCl

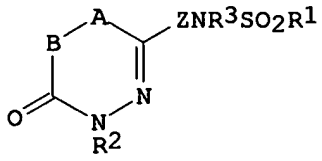
L8 ANSWER 58 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:435618 CAPLUS
DN 121:35618
TI Pyridazinone derivatives and processes for preparing them
IN Ishida, Akihoko; Homma, Koichi; Kono, Harumichi; Tamura, Koji; Sasaki, Yasuhiko
PA Tanabe Seiyaku Co., Ltd., Japan
SO Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 579059 | A1 | 19940119 | EP 1993-110611 | 19930702 |

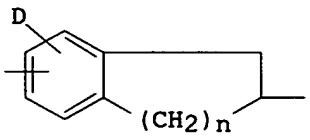
| | | | | | |
|---|---|---|---|---|---|
| | EP 579059 | B1 | 19990512 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | JP 06016663 | A2 | 19940125 | JP 1992-215354 | 19920702 |
| | CA 2099743 | AA | 19940103 | CA 1993-2099743 | 19930629 |
| | JP 06073020 | A2 | 19940315 | JP 1993-159338 | 19930629 |
| | AT 179972 | E | 19990515 | AT 1993-110611 | 19930702 |
| | US 5739132 | A | 19980414 | US 1996-767444 | 19961216 |
| PRAI | JP 1992-215354 | A | 19920702 | | |
| | JP 1992-215355 | A | 19920702 | | |
| | US 1993-83489 | B1 | 19930630 | | |

OS MARPAT 121:35618

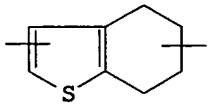
GI



I



II



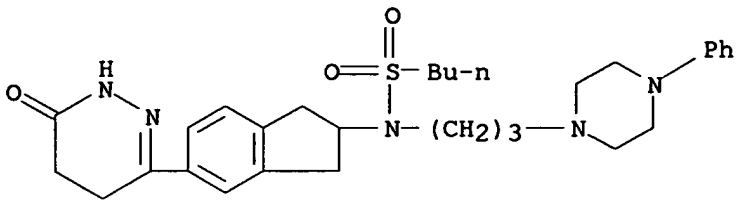
III

AB Pyridazinones I wherein (1) R1 is a substituted or unsubstituted C1-10 alkyl, a C3-6 cycloalkyl, a lower alkenyl, a heterocyclic group having N, O or S atom or camphor-10-yl; R3 is hydrogen, a substituted or unsubstituted lower alkyl or a lower alkenyl; or R1 and R3 are bonded at terminal ends thereof to form a lower alkylene; and Z is a group represented by II where n is 1 or 2; and D is hydrogen or a halogen; or (2) R1 is a substituted or unsubstituted C1-10 alkyl, a substituted or unsubstituted Ph, a C3-6 cycloalkyl, a lower alkenyl, a heterocyclic group having N, O or S atom or camphor-10-yl; R3 is hydrogen, a substituted or unsubstituted lower alkyl or a lower alkenyl; or R1 and R3 are bonded at terminal ends thereof to form a lower alkylene; and Z is a group represented by III and R2 is hydrogen, a substituted or unsubstituted lower alkyl, an aryl or a lower alkenyl; and -A-B- is an ethylene or vinylene each of which may be substituted by 1 or 2 groups selected from the group consisting of a lower alkyl and Ph group, or a pharmaceutically acceptable salt thereof were prepd. and are useful for protecting from endotoxin shock and curing nephritis. Thus, mice treated with 2-methylsulfonylamino-5-[4,5-dihydropyridazin-3(2H)-on-6-yl]indan (prepd. by methanesulfonylation of 2-amino-5-[4,5-dihydropyridazin-3(2H)-on-6-yl]indan) had 100% survival rate vs. a control when infected with an endotoxin (lipopolysaccharide) derived from Escherichia coli.

IT **172680-06-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for endotoxin shock protection and nephritis treatment)

RN 172680-06-7 CAPLUS

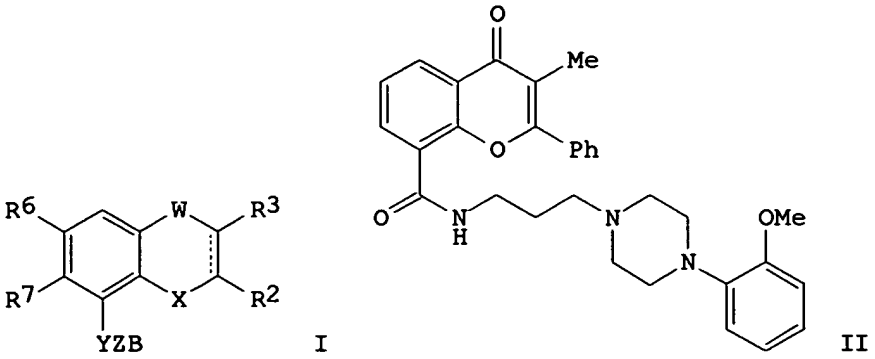
CN 1-Butanesulfonamide, N-[2,3-dihydro-5-(1,4,5,6-tetrahydro-6-oxo-3-pyridazinyl)-1H-inden-2-yl]-N-[3-(4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 59 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:106770 CAPLUS
DN 120:106770
TI Heterobicyclic compounds (flavoxate analogs) as antagonists of .alpha.1-adrenergic and 5-HT1A receptors
IN Leonardi, Amedeo; Motta, Gianni; Riva, Carlo; Testa, Rodolfo
PA Recordati S.A. Chemical and Pharmaceutical Co., Switz.; Recordati Industria Chimica e Farmaceutica S.p.a.
SO Eur. Pat. Appl., 109 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 558245 | A1 | 19930901 | EP 1993-301264 | 19930222 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| | US 5403842 | A | 19950404 | US 1992-888775 | 19920526 |
| | CA 2090156 | AA | 19930826 | CA 1993-2090156 | 19930223 |
| | WO 9317007 | A1 | 19930902 | WO 1993-EP420 | 19930223 |
| | W: AU, BG, CA, CZ, FI, HU, KR, LK, NO, NZ, PL, RO, RU, SK, UA | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | AU 9336296 | A1 | 19930913 | AU 1993-36296 | 19930223 |
| | HU 72448 | A2 | 19960429 | HU 1994-2443 | 19930223 |
| | RO 112111 | B3 | 19970530 | RO 1994-1404 | 19930223 |
| | PL 175556 | B1 | 19990129 | PL 1993-304889 | 19930223 |
| | RU 2128656 | C1 | 19990410 | RU 1994-43324 | 19930223 |
| | SK 280143 | B6 | 19990910 | SK 1994-1007 | 19930223 |
| | IL 104824 | A1 | 19991222 | IL 1993-104824 | 19930223 |
| | AU 9333773 | A1 | 19930826 | AU 1993-33773 | 19930224 |
| | AU 660067 | B2 | 19950608 | | |
| | ZA 9301278 | A | 19931118 | ZA 1993-1278 | 19930224 |
| | LT 3038 | B | 19940925 | LT 1993-354 | 19930224 |
| | LV 10099 | B | 19950220 | LV 1993-136 | 19930224 |
| | JP 06009606 | A2 | 19940118 | JP 1993-36605 | 19930225 |
| | TW 382628 | B | 20000221 | TW 1993-82103988 | 19930520 |
| | CN 1079738 | A | 19931222 | CN 1993-105852 | 19930526 |
| | CN 1040434 | B | 19981028 | | |
| | US 5474994 | A | 19951212 | US 1993-67861 | 19930526 |
| | FI 9403876 | A | 19940823 | FI 1994-3876 | 19940823 |
| | NO 9403140 | A | 19940825 | NO 1994-3140 | 19940825 |
| PRAI | IT 1992-MI408 | A | 19920225 | | |
| | US 1992-888775 | A | 19920526 | | |
| | EP 1993-301264 | A | 19930222 | | |
| | WO 1993-EP420 | A | 19930223 | | |

OS MARPAT 120:106770
GI



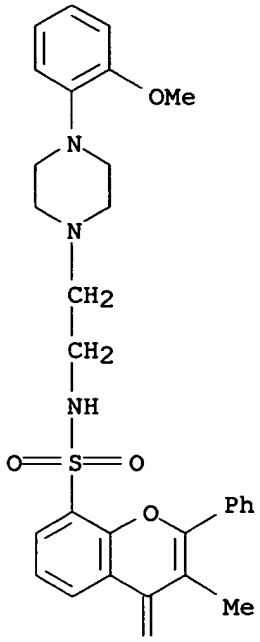

AB Title compds. I [dotted line = optional double bond; X = O, S, imino, alkylimino, S(O), S(O)2; W = bond, CO, C(S), CH2, CH(OH); R2 = H, (un)substituted alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aroyl; R3 = H, alkyl, hydroxyalkyl, alkoxyalkyl, aralkoxyalkyl, Ph, OH, alkoxy, aralkoxy; R6 = H, halo, NO2, (un)substituted NH2, cyano, OH, alkoxy, alkyl; R7 = H, alkoxy; Y = 49 bivalent functional groups such as CO, CO2, CONH, CH:CH, CH2, CH2NH, CH2O, O, S, SO2NH, etc.; Z = C1-6 alkylene with 1 optional OH substituent; B = various complex amine-contg. groups including substituted piperazines, piperidines, phenoxyalkylamines, etc.] and their prodrugs, N-oxides, and salts are claimed, with approx. 130 synthetic examples and 100 intermediate prepns. For example, 3-methyl-4-oxo-2-phenyl-4H-1-benzopyran-8-carbonyl chloride was amidated with H2N(CH2)3OH, and the resulting N-(3-hydroxypropyl) amide was converted to the N-(3-chloropropyl) amide by SOCl2. Condensation of this with 1-(2-methoxyphenyl)piperazine at 180.degree. gave title compd. II. I inhibited .alpha.1 receptor binding ([3H]-prazosin), 5-HT1A receptor binding ([3H]-8-OH-DPAT), and K+-induced contraction of isolated rat bladder, with different I showing different degrees and combinations of activity. For example, II had IC50 values of 29 nM, 9 nM, and 2.9-3.0 .mu.M in the 3 tests, whereas flavoxate was inactive in the receptor tests and only had IC50 of 13 .mu.M in the bladder test. Some I and esp. II showed high selectivity for urethral spasmolytic activity over antihypertensive activity in dogs.

IT **152735-59-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. as .alpha.1-adrenergic and/or 5-HT1A receptor antagonist)

RN 152735-59-6 CAPLUS

CN 4H-1-Benzopyran-8-sulfonamide, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-methyl-4-oxo-2-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



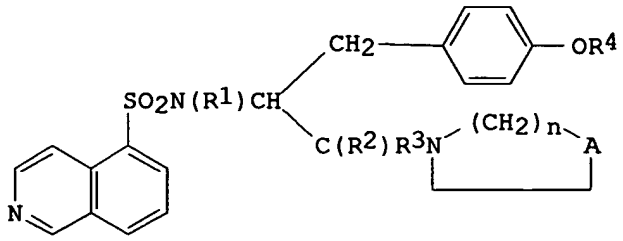

PAGE 2-A


● HCl

L8 ANSWER 60 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1993:641393 CAPLUS
DN 119:241393
TI Isoquinoline sulfonamide derivatives for anti-ulcer agents
IN Hidaka, Hiroyoshi; Ishikawa, Tomohiko
PA Japan
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5244895 | A | 19930914 | US 1992-883344 | 19920515 |
| PRAI | JP 1991-8580 | A | 19910515 | | |

OS MARPAT 119:241393
GI



I

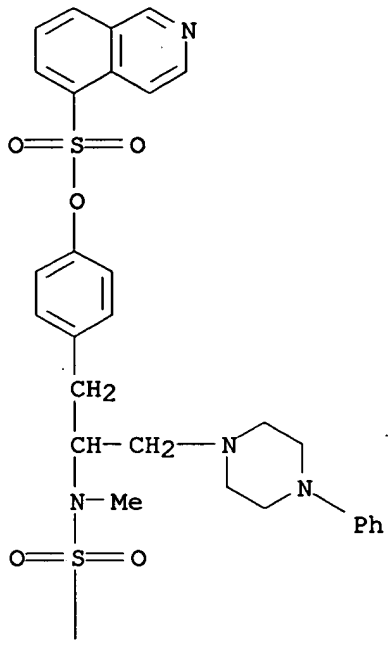
AB The anti-ulcer agents of the invention are I [R1 = H, (substituted) C1-2 alkyl; R2, R3 = H or together form oxo; R4 = H, Me, isoquinoline sulfonyl; n = 2, 3; A = NR5 CHR5 (R5 = (substituted) Ph, (substituted) benzyloxycarbonyl] or a physiol. allowable acid addn. salt thereof. Twelve specific I are claimed; and prepn. of 3 I is described. Thus, N-[N,O-bis(5-isoquinoline sulfonyl)-N-methyl-tyrosyl]-4-phenylpiperazine (II) (prepn. given) and 15 other I were tested in an anti-gastric juice secretion test and an anti-aspirin ulcer test. Tablet and injection formulations of II phosphate are included.

IT **130962-59-3**
RL: BIOL (Biological study)
(ulcer inhibitor)

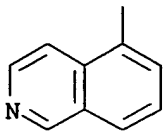
RN 130962-59-3 CAPLUS

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)methylamino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

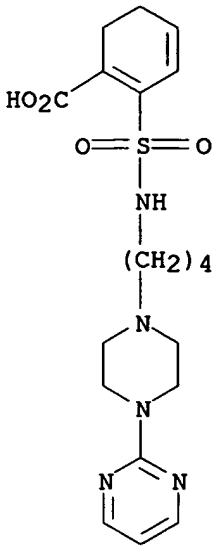
PAGE 1-A



PAGE 2-A



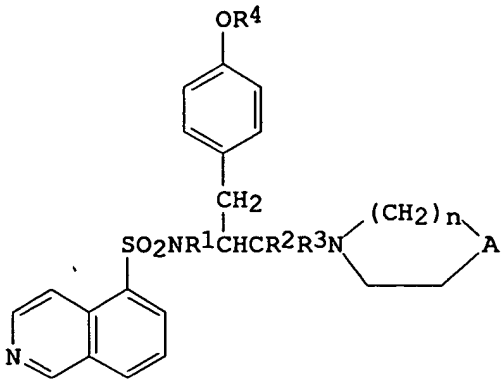
L8 ANSWER 61 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1993:480377 CAPLUS
DN 119:80377
TI Analysis of new serotonergic anxiolytics by liquid chromatography
AU Farina, A.; Doldo, A.; Quaglia, M. G.
CS Lab. Chim. Farm., Ist. Super. Sanita, Rome, 00161, Italy
SO Journal of Pharmaceutical and Biomedical Analysis (1992), 10(10-12), 889-93
CODEN: JPBADA; ISSN: 0731-7085
DT Journal
LA English
AB A simple isocratic procedure was developed for the anal. of new serotonergic anxiolytics and related compds. in bulk, pharmaceuticals, and in biol. samples. The system may be applied for the assay of other serotonergic anxiolytics of related structure such as buspirone. The HPLC assay utilized a reversed-phase C18 column, a mobile phase consisting of a mixt. (55:45) of (A) buffer potassium dihydrogen phosphate (0.05M) contg. sodium lauryl sulfate (0.005M) and (B) MeCN. A fluorescence detection was used with .lambda.ex 237 nm; .lambda.em 374 nm. The accuracy, precision and sensitivity of the proposed method were established. Std. curves were linear with respect to concn. in the range 0.05-7.5 .mu.g mL-1. The method also allowed the sepn. and identification of related compds. at concns. <0.01%.
IT **149095-55-6**
RL: PROC (Process)
(sepn. of, as impurity from serotonergic anxiolytic by HPLC)
RN 149095-55-6 CAPLUS
CN 1,3-Cyclohexadiene-1-carboxylic acid, 2-[[[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]amino]sulfonyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 62 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1993:124410 CAPLUS
DN 118:124410
TI Substituted 5-isoquinolinesulfonamides as antiulcer agent
IN Hidaka, Hiroyoshi; Ishikawa, Tomohiko
PA Japan
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 513691 | A1 | 19921119 | EP 1992-107816 | 19920508 |
| | EP 513691 | B1 | 19960731 | | |
| | R: DE, FR, GB | | | | |
| | JP 06009402 | A2 | 19940118 | JP 1991-138580 | 19910515 |
| PRAI | JP 1991-138580 | A | 19910515 | | |

OS MARPAT 118:124410
GI



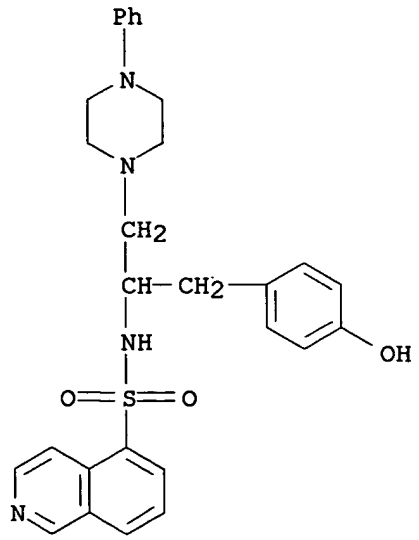
I

AB Title compds. I [R1 = H, (substituted) C1-2 alkyl; R2, R3 = H, R2R3 = O; R4 = H, Me, isoquinolinylsulfonyl; n = 2, 3; A = R5N, R5CH wherein R5 = (substituted) Ph, PhCH2O2C] or a salt thereof, some of which were prepd., are antiulcer agents. N-(tert-Butoxycarbonyl)tyrosine Me esters in THF and DMF was added to NaH followed by MeOCH2CH2OCH2Cl to give N-(tert-butoxycarbonyl)-O-(2-methoxyethoxymethyl)tyrosinol which in CCl4 was reacted with Ph3P followed by 4-(3,4-dichlorobenzyloxy)piperidine to give N-[2-amino-3-(p-hydroxyphenyl)propyl]-4-(3,4-dichlorobenzyloxy)piperidine which in THF was treated 5-isoquinolinesulfonyl chloride HCl to give I (R1-R4 = H, n = 2, A = 3,4-Cl2C6H3CH2OCH) (II). In test for antiaspirin ulcer test, II at 100 mg/kg showed 65% inhibition. A tablet and aseptic injection formulation comprising an analog of II.phosphate is given.

IT **130962-61-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(antiulcer agent)

RN 130962-61-7 CAPLUS

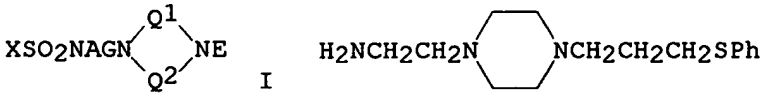
CN 5-Isoquinolinesulfonamide, N-[1-[(4-hydroxyphenyl)methyl]-2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 63 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1993:80951 CAPLUS
DN 118:80951
TI Preparation of sulfonamide derivatives containing heterocyclyl groups
IN Kajihara, Akiro; Asano, Toshio
PA Asahi Kasei Kogyo K. K., Japan
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9214712 | A1 | 19920903 | WO 1992-JP146 | 19920213 |
| | W: CA, NO, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | JP 05001037 | A2 | 19930108 | JP 1991-261394 | 19910913 |
| | CA 2089128 | AA | 19920814 | CA 1992-2080128 | 19920213 |
| | EP 525203 | A1 | 19930203 | EP 1992-904985 | 19920213 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE | | | | |
| | US 5326870 | A | 19940705 | US 1992-927493 | 19920929 |
| | NO 9203808 | A | 19921211 | NO 1992-3808 | 19920930 |
| | NO 178066 | B | 19951009 | | |
| | NO 178066 | C | 19960117 | | |
| PRAI | JP 1991-19761 | A | 19910213 | | |
| | WO 1992-JP146 | W | 19920213 | | |

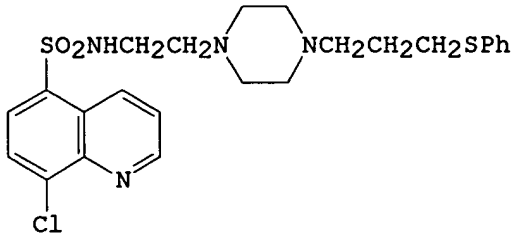
OS MARPAT 118:80951
GI




I




II

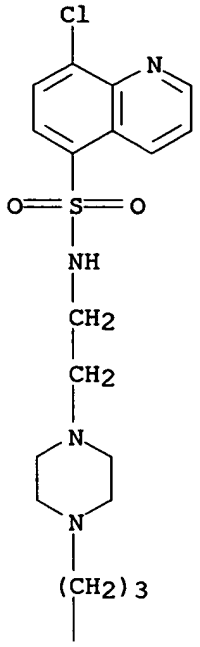



III

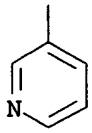
AB The title compds. [I; A = H, alkyl; E = alkyl, alkoxyalkyl, aryloxyalkyl, etc.; G = alkylene; Q1, Q2 = (CH2)2, (CH2)3; X = quinoline, isoquinoline, benzothiazole, 4-oxoquinazoline residue], useful as antiasthmatics, are prepd. 8-Chloro-5-quinolinesulfonic acid was refluxed with SOCl2 in DMF and the resultant sulfonyl chloride was treated with piperazine deriv. II and Et3N in CH2Cl2 at 20.degree. to give 72% sulfonamide III, which showed 82% inhibition of histamine-induced vasoconstriction at 0.1 mg/kg i.v. in guinea pigs.

IT **145708-53-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antiasthmatic agent)
RN 145708-53-8 CAPLUS
CN 5-Quinolinesulfonamide, 8-chloro-N-[2-[4-[3-(3-pyridinyl)propyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

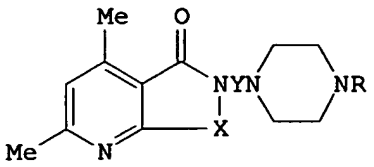
PAGE 1-A



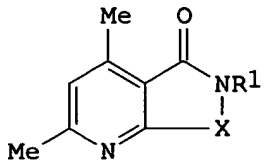

PAGE 2-A



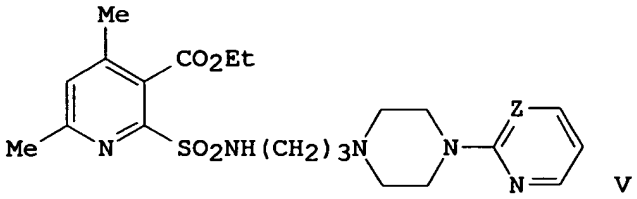

L8 ANSWER 64 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1993:80890 CAPLUS
DN 118:80890
TI Synthesis and biological evaluation of some piperazine derivatives of isothiazolo[5,4-b]pyridin-3-one and its 1,1-dioxide
AU Malinka, Wieslaw
CS Dep. Drug Chem., Sch. Med., Wroclaw, 50137, Pol.
SO Acta Poloniae Pharmaceutica (1991), 48(1-2), 19-23
CODEN: APPHAX; ISSN: 0001-6837
DT Journal
LA English
GI



I



II



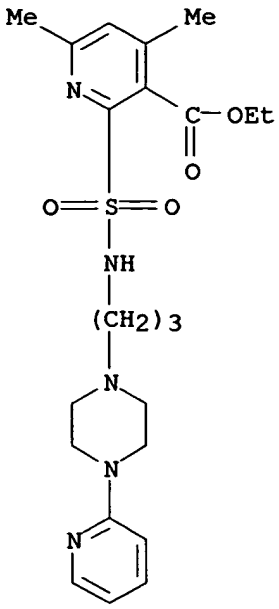
V

AB Twenty-one piperazinylalkyl-substituted isothiazolopyridine derivs. I were prepd. for screening as CNS active agents. Thus, I (Y = CH2, X = S, R = Me, 2-, 3-, and 4-ClC6H4, 2-pyridyl, and 2-pyrimidinyl) were obtained in 55-85% yields in the Mannich reaction of II (X = S, R1 = H, III) with CH2O and the appropriately 4-R-substituted piperazine. I (Y = CH2CHOHCH2, X = S, R as above plus Ph) were prepd. in 60-83% yields from III via II (X = S, R1 = 2,3-epoxypropyl) and subsequent oxirane ring opening with the appropriately 4-R-substituted piperazine. I (Y = (CH2)2, X = SO2, R = Me, Ph, 2-pyridyl, and 2-pyrimidinyl) were prepd. in 54-74% yields from II (X = SO2, R1 = H, IV) via II [X = SO2, R1 = (CH2)2OH], the tosyl deriv. of which was treated with the 4-R-substituted piperazine, whereas the analogously R-substituted I [Y = (CH2)3, X = SO2] were prepd. in 50-70% yields directly from IV in the reaction with 4-R-1-(3-chloropropyl)piperazine. When 4-(2-pyridyl)- and 4-(2-pyrimidinyl)piperazine were used in the latter reaction, some V (Z = CH and N, resp.) were formed.

IT **145787-23-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

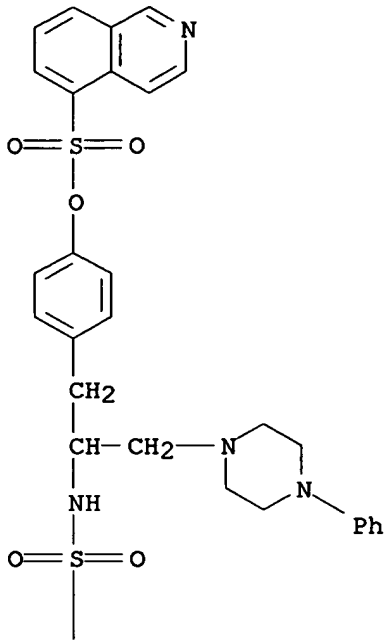
RN 145787-23-1 CAPLUS

CN 3-Pyridinecarboxylic acid, 4,6-dimethyl-2-[[[3-[4-(2-pyridinyl)-1-piperazinyl]propyl]amino]sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

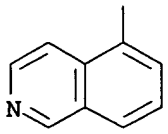


L8 ANSWER 65 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1993:16135 CAPLUS
DN 118:16135
TI Inhibition of insulin secretion by KN-62, a specific inhibitor of the multifunctional calcium/calmodulin-dependent protein kinase II
AU Wenham, Robert M.; Landt, Michael; Walters, Steven M.; Hidaka, Hiroyoshi; Easom, Richard A.
CS Dep. Biochem. Mol. Biol., Texas Coll. Osteop. Med., Fort Worth, TX, 76107, USA
SO Biochemical and Biophysical Research Communications (1992), 189(1), 128-33
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB The effects of KN-62, a specific inhibitor of Ca2+/calmodulin-dependent protein kinase II (CamPKII), on insulin secretion and protein phosphorylation were studied in rat pancreatic islets and RINm5F cells. KN-62 was found to dose-dependently inhibit autophosphorylation of CamPKII in subcellular prepns. of RINm5F cells (K0.5 = 3.1 mM), but had no effect on protein kinase C or myosin light chain kinase activity. KN-62, but not the inactive analog KN-04, dose-dependently inhibited glucose-induced insulin release (K0.5 = 1.5 .mu.M) in a manner similar to the inhibition of CaMPKII autophosphorylation. KN-62 (10 .mu.M) inhibited carbachol (in the presence of (mM glucose) and potassium-stimulated insulin secretion from islets by 53% and 59%, resp. These results support a role of CamPKII in glucose-sensitive insulin secretion.
IT **129695-80-3**, KN-04
RL: BIOL (Biological study)
(protein kinase response to, in pancreatic .beta. cells)
RN 129695-80-3 CAPLUS
CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



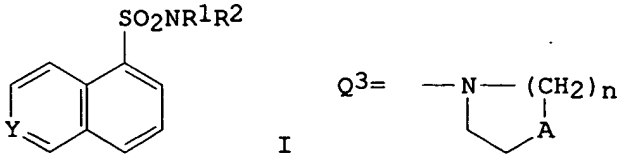
L8 ANSWER 66 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:20955 CAPLUS
DN 116:20955
TI Preparation of isoquinoline-5-sulfonamides and analogs as blood vessel relaxants
IN Hidaka, Hiroyoshi; Ishikawa, Tomohiko; Hagiwara, Masatoshi; Inoue, Tsutomu; Naitoh, Kenji; Sakuma, Osamu; Yuasa, Masayuki; Morita, Tadashi; Toshioka, Tadashi; et al.
PA Tobishi Pharmaceutical Co., Ltd., Japan
SO Ger. Offen., 86 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE 3942114 | A1 | 19900628 | DE 1989-3942114 | 19891220 |
| | DE 3942114 | C2 | 19970904 | | |
| | CA 2005741 | AA | 19900626 | CA 1989-2005741 | 19891215 |
| | CA 2005741 | C | 19980602 | | |

| | | | | | |
|---|---|---|---|---|---|
| | JP 02256666 | A2 | 19901017 | JP 1989-325959 | 19891218 |
| | JP 2886225 | B2 | 19990426 | | |
| | SE 8904261 | A | 19900627 | SE 1989-4261 | 19891219 |
| | SE 503081 | C2 | 19960318 | | |
| | US 5081246 | A | 19920114 | US 1989-453623 | 19891220 |
| | DE 3943678 | C2 | 19991125 | DE 1989-3943678 | 19891220 |
| | GB 2228933 | A1 | 19900912 | GB 1989-28895 | 19891221 |
| | GB 2228933 | B2 | 19930331 | | |
| | CH 680441 | A | 19920831 | CH 1989-4647 | 19891221 |
| | DK 8906662 | A | 19900627 | DK 1989-6662 | 19891222 |
| | DK 175678 | B1 | 20050117 | | |
| | FR 2640973 | A1 | 19900629 | FR 1989-17091 | 19891222 |
| | FR 2640973 | B1 | 19920327 | | |
| | NL 8903143 | A | 19900716 | NL 1989-3143 | 19891222 |
| | NL 193726 | B | 20000403 | | |
| | NL 193726 | C | 20000804 | | |
| | ES 2029759 | A6 | 19920901 | ES 1989-4335 | 19891222 |
| | AT 8902935 | A | 19940215 | AT 1989-2935 | 19891222 |
| | CN 1044098 | A | 19900725 | CN 1989-109843 | 19891226 |
| | CN 1025618 | B | 19940810 | | |
| | JP 03007262 | A2 | 19910114 | JP 1990-11719 | 19900123 |
| | JP 3048590 | B2 | 20000605 | | |
| | JP 03047170 | A2 | 19910228 | JP 1990-52686 | 19900306 |
| | JP 3078295 | B2 | 20000821 | | |
| | US 5216150 | A | 19930601 | US 1991-758808 | 19910912 |
| | GB 2248235 | A1 | 19920401 | GB 1991-22595 | 19911024 |
| | GB 2248235 | B2 | 19930331 | | |
| | US 5245034 | A | 19930914 | US 1992-856178 | 19920323 |
| | CN 1074214 | A | 19930714 | CN 1992-115101 | 19921230 |
| | CN 1028638 | B | 19950531 | | |
| | NL 9900004 | A | 19990901 | NL 1999-4 | 19990517 |
| | NL 194549 | B | 20020301 | | |
| | NL 194549 | C | 20020702 | | |
| PRAI | JP 1988-325910 | A | 19881226 | | |
| | JP 1989-76419 | A | 19890330 | | |
| | JP 1989-87868 | A | 19890410 | | |
| | DE 1989-3942114 | A3 | 19891220 | | |
| | US 1989-453623 | A3 | 19891220 | | |
| | GB 1989-28895 | A3 | 19891221 | | |
| | NL 1989-3143 | A3 | 19891222 | | |
| | CN 1989-109843 | A | 19891226 | | |
| | US 1991-758808 | A3 | 19910912 | | |

OS MARPAT 116:20955

GI




I

AB The title compds. [I; R1 = H, CHO, (halophenyl)propargyl, (un)substituted alkyl, aralkyl, Ph; R2 = WNR3CHR4XmQ1, CH(CR12R13R)CH2Q2, W = alkylene, (un)substituted phenylenediyl, or a combination of these; R3 = R1; R1R3 =

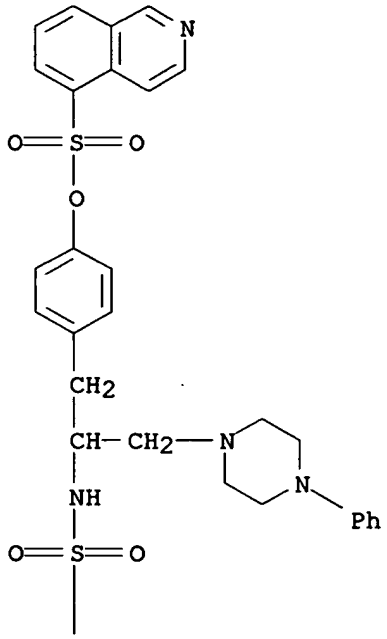
alkylene; R4 = H, alkyl; X = CH:CH, C.tplbond.C; Q1, Q2 = (un)substituted Ph, naphthyl, heterocyclyl; R12, R13 = H; R12R13 = O; R = Q3; A = CO, (un)substituted CH2, NH, etc.; R1R3 = alkylene; Y = N, CH, CMe; m, n = 1-3] were prepd. Thus, I (R1 = H, Y = N) (II; R2 = CH2CH2NH2) was stirred 1 h with 4-ClC6H4CH:CHCHO in MeOH after which NaBH4 was added and stirring continued 30 min to give II (R2 = CH2CH2NR5CH2CH:CHC6H4Cl-4) (III; R5 = H) which was methylated to give III (R5 = Me). The latter had EC50 of 0.19 .mu.M for relaxation of rabbit aorta strips in vitro.

IT **129695-80-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as blood vessel relaxant)

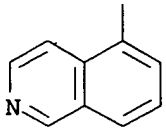
RN 129695-80-3 CAPLUS

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

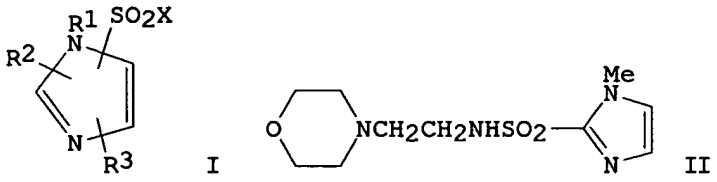


L8 ANSWER 67 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:632247 CAPLUS
DN 115:232247
TI Preparation of imidazolesulfonamides as antithrombotic agents

IN Graeve, Rolf; Okyayuz-Baklouti, Ismahan; Seiffge, Dirk
PA Hoechst A.-G., Germany
SO Ger. Offen., 39 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE 4004061 | A1 | 19910814 | DE 1990-4004061 | 19900210 |
| | EP 442348 | A2 | 19910821 | EP 1991-101497 | 19910205 |
| | EP 442348 | A3 | 19920304 | | |
| | EP 442348 | B1 | 19960717 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | AT 140452 | E | 19960815 | AT 1991-101497 | 19910205 |
| | ES 2090150 | T3 | 19961016 | ES 1991-101497 | 19910205 |
| | FI 9100602 | A | 19910811 | FI 1991-602 | 19910207 |
| | BR 9100520 | A | 19911029 | BR 1991-520 | 19910207 |
| | CA 2035988 | AA | 19910811 | CA 1991-2035988 | 19910208 |
| | NO 9100496 | A | 19910812 | NO 1991-496 | 19910208 |
| | AU 9170848 | A1 | 19910815 | AU 1991-70848 | 19910208 |
| | AU 634342 | B2 | 19930218 | | |
| | HU 56549 | A2 | 19910930 | HU 1991-415 | 19910208 |
| | HU 207997 | B | 19930728 | | |
| | ZA 9100948 | A | 19911030 | ZA 1991-948 | 19910208 |
| | JP 04316561 | A2 | 19921106 | JP 1991-60750 | 19910208 |
| | JP 3026847 | B2 | 20000327 | | |
| | US 5232922 | A | 19930803 | US 1991-652606 | 19910208 |
| | CN 1053919 | A | 19910821 | CN 1991-100969 | 19910209 |
| | US 5356922 | A | 19941018 | US 1993-57887 | 19930507 |
| PRAI | DE 1990-4004061 | A | 19900210 | | |
| | US 1991-652606 | A3 | 19910208 | | |

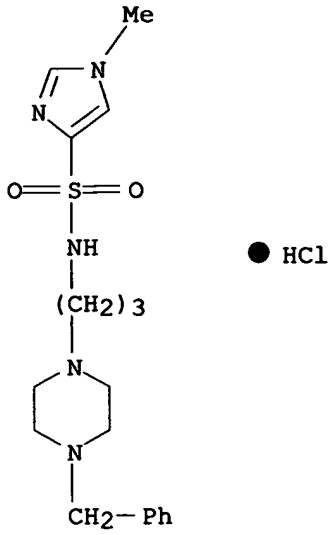
OS MARPAT 115:232247
GI




AB The title compds. [I; R1 = alkyl; R2,R3 = H, halo, alkyl; X = OH, NR4R5; R4 = H, (un)substituted alkyl; R5 = phenylalkyl, (un)substituted alkyl, etc.] were prepd. Thus, 1-methyl-2-imidazolesulfonyl chloride was condensed with 2-morpholinoethylamine to give title compd. II.HCl which gave 45% inhibition of laser-induced thromboses in rats at 10 mg/kg orally.

IT **137048-49-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antithrombotic agent)

RN 137048-49-8 CAPLUS
CN 1H-Imidazole-4-sulfonamide, 1-methyl-N-[3-[4-(phenylmethyl)-1-piperazinyl]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



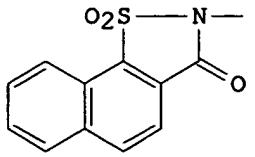
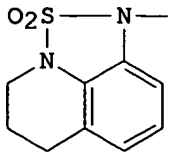
L8 ANSWER 68 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:583316 CAPLUS
DN 115:183316
TI Preparation and formulation of thiadiazolo[4,3,2-ij]quinolines and analogs as serotonin antagonists
IN Comte, Marie Therese; Gueremy, Claude; Malleron, Jean Luc; Peyronnel, Jean Francois; Truchon, Alain
PA Rhone-Poulenc Sante, Fr.
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 433149 | A2 | 19910619 | EP 1990-403502 | 19901210 |
| | EP 433149 | A3 | 19920318 | | |
| | EP 433149 | B1 | 19940216 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | FR 2655652 | A1 | 19910614 | FR 1989-16459 | 19891213 |
| | FR 2655652 | B1 | 19940610 | | |
| | FR 2662696 | A2 | 19911206 | FR 1990-6943 | 19900605 |
| | AT 101612 | E | 19940315 | AT 1990-403502 | 19901210 |
| | ES 2062465 | T3 | 19941216 | ES 1990-403502 | 19901210 |
| | CA 2032104 | AA | 19910614 | CA 1990-2032104 | 19901212 |
| | FI 9006108 | A | 19910614 | FI 1990-6108 | 19901212 |
| | NO 9005368 | A | 19910614 | NO 1990-5368 | 19901212 |
| | AU 9067981 | A1 | 19910620 | AU 1990-67981 | 19901212 |
| | AU 643241 | B2 | 19931111 | | |
| | HU 56566 | A2 | 19910930 | HU 1990-8242 | 19901212 |
| | HU 209301 | B | 19940428 | | |
| | ZA 9009982 | A | 19911030 | ZA 1990-9982 | 19901212 |
| | JP 03255063 | A2 | 19911113 | JP 1990-410112 | 19901213 |
| | US 5130313 | A | 19920714 | US 1990-627101 | 19901213 |
| PRAI | FR 1989-16459 | A | 19891213 | | |

| | | | |
|---|---|---|---|
| | FR 1990-6943 | A | 19900605 |
| | EP 1990-403502 | A | 19901210 |

OS MARPAT 115:183316

GI

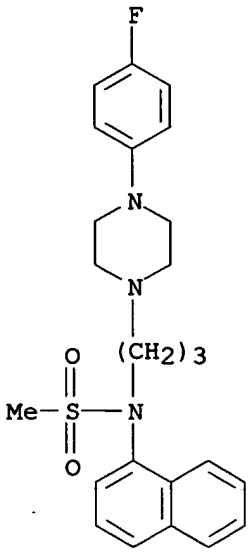
Q1=  Q2= 

AB R2R3N(CH2)nR1 [I; R1 = (substituted) 1,2,3,6-tetrahydro-1-pyridyl, 1-piperazinyl, etc.; R2 = SO2R4; R4 = alkyl, Ph; R3 = Ph, naphthyl; or NR2R3 = Q1, Q2, etc.; n = 2 to 4] were prepd. I are useful as serotonin antagonists (no data). Treatment of 5,6-dihydro-1H,4H-1,2,5-thiadiazolo[4,3,2-ij]quinoline 2,2-dioxide with NaH, followed by reaction with 1-(3-chloropropyl)-4-phenyl-1,2,3,6-tetrahydropyridine, gave 1-[3-(4-phenyl-1,2,3,6-tetrahydro-1-pyridyl)propyl]-5,6-dihydro-1H,4H-1,2,5-thiadiazolo[4,3,2-ij]quinoline 2,2-dioxide.

IT **136481-56-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 136481-56-6 CAPLUS

CN Methanesulfonamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-N-1-naphthalenyl- (9CI) (CA INDEX NAME)



L8 ANSWER 69 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1991:429363 CAPLUS

DN 115:29363

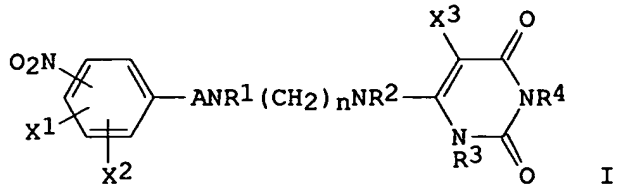
TI Preparation of pyrimidinedione derivatives as antiarrhythmic agents

IN Katakami, Tsutomu; Yokoyama, Tatsuro; Miyamoto, Michihiko; Mori, Haruki; Kawauchi, Nobuya; Nobori, Tadahito; Sannohe, Kunio; Kamiya, Joji; Ishii,

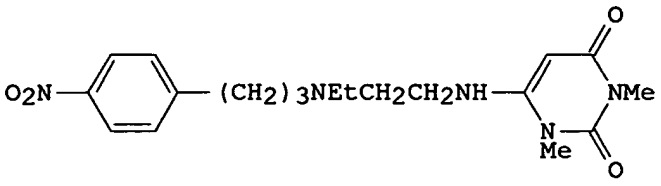
Masaaki; Yoshihara, Kanji
PA Mitsui Toatsu Chemicals, Inc., Japan
SO Eur. Pat. Appl., 225 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 369627 | A2 | 19900523 | EP 1989-311135 | 19891027 |
| | EP 369627 | A3 | 19901212 | | |
| | EP 369627 | B1 | 19941221 | | |
| | R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE | | | | |
| | CA 2001389 | AA | 19900429 | CA 1989-2001389 | 19891024 |
| | CA 2001389 | C | 19980210 | | |
| | US 5008267 | A | 19910416 | US 1989-425730 | 19891024 |
| | DK 8905357 | A | 19900430 | DK 1989-5357 | 19891027 |
| | DK 170203 | B1 | 19950612 | | |
| | NO 8904299 | A | 19900430 | NO 1989-4299 | 19891027 |
| | NO 174711 | B | 19940314 | | |
| | NO 174711 | C | 19940622 | | |
| | AU 8943869 | A1 | 19900531 | AU 1989-43869 | 19891027 |
| | AU 613805 | B2 | 19910808 | | |
| | HU 52764 | A2 | 19900828 | HU 1989-5468 | 19891027 |
| | HU 210780 | B | 19950728 | | |
| | ES 2066000 | T3 | 19950301 | ES 1989-311135 | 19891027 |
| | FI 95245 | B | 19950929 | FI 1989-5121 | 19891027 |
| | FI 95245 | C | 19960110 | | |
| | JP 03173873 | A2 | 19910729 | JP 1989-279827 | 19891030 |
| | JP 06088982 | B4 | 19941109 | | |
| | JP 03112948 | A2 | 19910514 | JP 1990-112709 | 19900427 |
| PRAI | JP 1988-271992 | A | 19881029 | | |
| | JP 1988-306840 | A | 19881206 | | |
| | JP 1988-306841 | A | 19881206 | | |
| | JP 1989-96416 | A | 19890418 | | |
| | JP 1989-96417 | A | 19890418 | | |
| | JP 1989-96418 | A | 19890418 | | |
| | JP 1989-229272 | A | 19890906 | | |
| | JP 1989-246317 | A | 19890925 | | |
| | JP 1989-246318 | A | 19890925 | | |

OS MARPAT 115:29363
GI



I



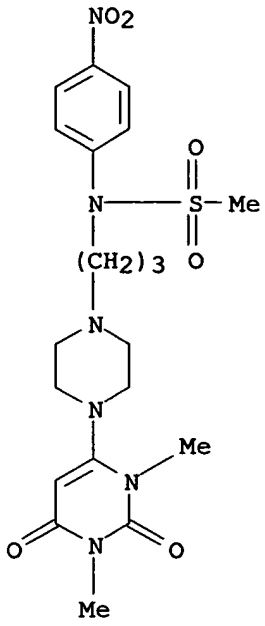
II

AB Title compds. I [A = (CH2)m, alkoxy, alkylthio, alkylaminocarbonyl, piperidinediyl, CH2NH, O2C, etc.; m = 0-4; R1, R2 = H, alkoxycarbonyl, (unsatd.)(substituted) alkyl, mono(di)alkylamino, alkoxy, (substituted) Ph, etc.; or R1R2 = alkylene and thus forming a heterocyclyl; R3, R4 = H, alkyl; X1, X2 = H, halo, alkyl, alkylcarbonyl, etc.; X3 = H, O2N, Me, cyano, etc.; n = 2,3] or a salt thereof are prepd. N-Ethyl-N-3-(4-nitrophenyl)propylamine (prepn. given) and 6-(1-aziridinyl)-1,3-dimethyl-2,4-(1H,3H)-pyrimidinedione (prepn. given) were concd. under reduced pressure and reacted with Amberylst to give the pyrimidinone II, as the HCl salt (III). In tests for pharmacol. activity by influence on myocardial action potential duration time (APD75) and influence on ventricular muscle refractory period (ERF) the dose of III at 1.0 .mu.g/mL showed ADP75 11% and ERP 16.7%. Pharmaceutical formulations of I are given.

IT **130634-73-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antiarrhythmic)

RN 130634-73-0 CAPLUS

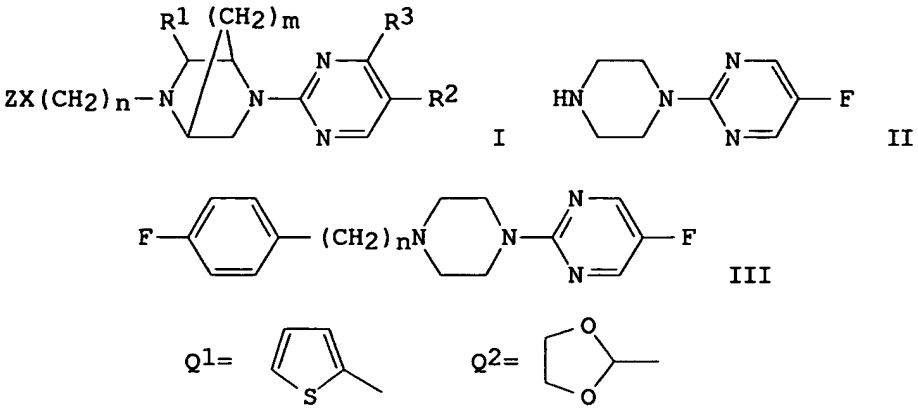
CN Methanesulfonamide, N-(4-nitrophenyl)-N-[3-[4-(1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-4-pyrimidinyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 70 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:247309 CAPLUS
DN 114:247309
TI Preparation of pyrimidylpiperazines as agents for treatment of brain and spinal cord ischemia
IN Yevich, Joseph P.; Dextraze, Pierre
PA Bristol-Myers Squibb Co., USA
SO Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 400661 | A1 | 19901205 | EP 1990-110399 | 19900531 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | US 4994460 | A | 19910219 | US 1990-503197 | 19900330 |
| | CA 2017596 | AA | 19901201 | CA 1990-2017596 | 19900525 |
| | JP 03047172 | A2 | 19910228 | JP 1990-141756 | 19900601 |
| PRAI | US 1989-360657 | A | 19890601 | | |
| | US 1990-503197 | A | 19900330 | | |

OS MARPAT 114:247309
GI

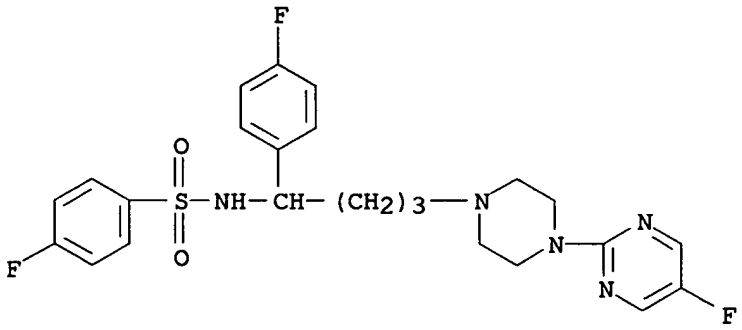



AB The title compds. I (Z = 4-FC6H4, Q1, naphthalenyl, etc.; X = O, S, SO2, etc.; Z and X taken together can be Q2; R1 = H, alkyl; R2 = halo; R3 = H, alkoxy, alkylthio; n = 1-3; and m = 0 or 1; a proviso is given) were prepd. A mixt. of piperazine II, 4-FC6H4(CH2)4Cl, K2CO3, and MeCN was refluxed for 40 h to give piperazine III (n = 4). III (n = 1) at 40 mg/kg i.p. gave protection (up to 25% survival) in rats subjected to the anoxic nitrogen test.

IT **133982-23-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of brain ischemia)

RN 133982-23-7 CAPLUS

CN Benzenesulfonamide, 4-fluoro-N-[1-(4-fluorophenyl)-4-[4-(5-fluoro-2-pyrimidinyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)




L8 ANSWER 71 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1991:228960 CAPLUS

DN 114:228960

TI 2-[[(4-Phenyl-1-piperazinyl)alkyl]amino]-5-ethynylpyrimidine derivatives, their intermediates, and preparation of the intermediates

IN Isobe, Toshio; Nagao, Takashi; Takashi, Yoshiho; Miyagaki, Mitsuhiro; Ito, Shigeru; Azuma, Hiroshi; Ishikawa, Masayuki

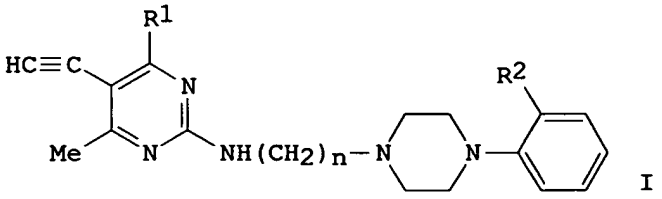
PA Shiratori Pharmaceutical Co., Ltd., Japan; Hitachi Chemical Co., Ltd.

SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF

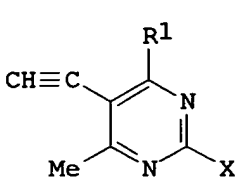
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 03007266 | A2 | 19910114 | JP 1989-140408 | 19890602 |
| | JP 2704231 | B2 | 19980126 | | |
| PRAI | JP 1989-140408 | | 19890602 | | |

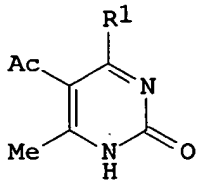
OS MARPAT 114:228960
GI



I



II

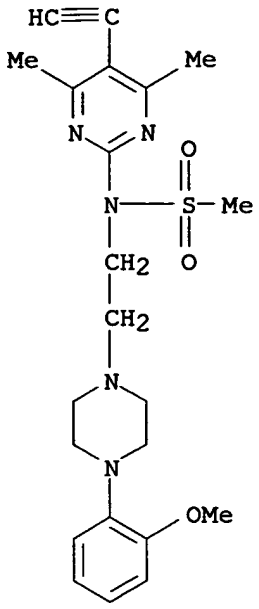


III

AB The title derivs. I [R1 = lower alkyl, (un)substituted phenyl; R2 = alkoxy; n = 2-4], useful as antihypertensives, their intermediates ethynylhalopyrimidiines II (X = halo), and a process for the prepn. of II by treatment of acetyldihydropyrimidinones III with halogenating agents are claimed. A mixt. of POCl3 and III (R1 = Me) was refluxed for 15.5 h to give 65% II (R1 = Me, X = Cl), which was further treated with 2-[4-(2-methoxyphenyl)-1-piperazinyl]ethylamine and Et3N in MeCN under reflux for 7 h to give 95% I (R1 = Me, R2 = OMe, n = 2) (IV). An aq. soln. of IV mesylate was applied to the right carotid of an anesthetized rabbit at 100 .mu.g/0.1 mL/kg; the antihypertensive activity was 12.5 mmH.

IT **133894-03-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antihypertensive)

RN 133894-03-8 CAPLUS
CN Methanesulfonamide, N-(5-ethynyl-4,6-dimethyl-2-pyrimidinyl)-N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 72 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1990:549578 CAPLUS
DN 113:149578
TI Effect of a new calcium-calmodulin-dependent protein kinase II inhibitor on GABA release in cerebrospinal fluid of the rat
AU Ishikawa, Naohisa; Hashiba, Yukihiro; Hidaka, Hiroyoshi
CS Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SO Journal of Pharmacology and Experimental Therapeutics (1990), 254(2), 598-602
CODEN: JPETAB; ISSN: 0022-3565
DT Journal
LA English
AB The role of Ca2+-calmodulin-dependent protein kinase II (CaM kinase II) in the central nervous system has been studied with special ref. to the effect of CaM kinase II inhibitor on GABA release. Two different selective inhibitors of Ca2+-calmodulin-dependent enzymes such as a calmodulin antagonist, W 7, and a newly synthesized selective inhibitor of CaM kinase II, KN 62 were used. N-[1-[p-(5-Isoquinolinesulfonyl)benzyl]-2-(4-phenylpiperazinyl)ethyl]-5-isoquinolinesulfonamide (KN 04), a deriv. of KN 62, which has a much lower inhibitory activity on the enzyme, was also synthesized for use as a control. Although i.v. injection of the drugs did not produce any effect, infusion of W 7 or KN 62 into the 4th ventricle of the rat caused hypertension and tachycardia, assocd. with the diminished rate of GABA release in cerebrospinal fluid. The ability of KN 62 to produce these effects was more potent than that of W 7. Intracisternal infusion of KN 04 influenced neither systemic blood pressure nor GABA release at the concn. up to 100 .mu.M. The same order of potencies of 3 agents (KN 62 > W 7 .mchgt. KN 04) has been obtained in their effects on either in vitro CaM kinase II activity, the in vivo autonomic nervous system, or the rate of GABA release. Thus, CaM kinase II inhibitors such as KN 62 administered into the 4th ventricle decreased the rate of GABA release into the cerebrospinal fluid, enhancing the autonomic nervous function, and these effects were closely related to

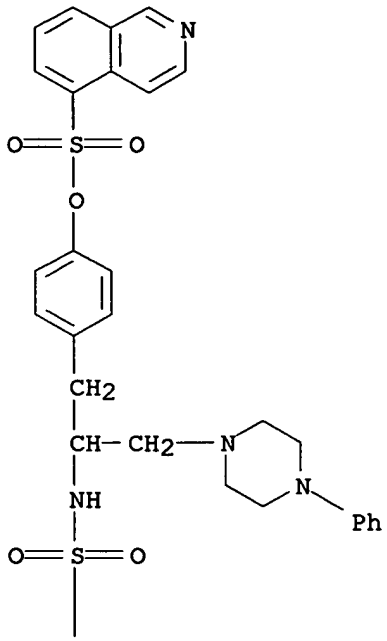
their inhibitory action on CaM kinase II activity.

IT **129695-80-3**, KN 04
RL: BIOL (Biological study)
(cardiovascular system and GABA release into cerebrospinal fluid responses to, calmodulin kinase II inhibition in relation to)

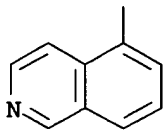
RN 129695-80-3 CAPLUS

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)amino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L8 ANSWER 73 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1990:139052 CAPLUS

DN 112:139052

TI Preparation of arylsulfonylpiperazines as antiinflammatories

IN Abou-Gharbia, Magid A.

PA American Home Products Corp., Japan

SO U.S., 4 pp.
CODEN: USXXAM

DT Patent

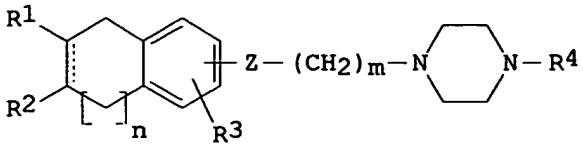
LA English

FAN.CNT 1

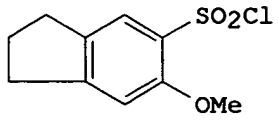
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 4857644 | A | 19890815 | US 1988-204459 | 19880609 |
| PRAI | US 1988-204459 | | 19880609 | | |

OS CASREACT 112:139052; MARPAT 112:139052

GI



I



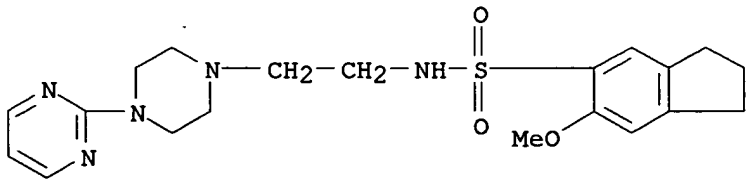
II

AB The title compds. [I; R1, R2 = H, C1-6 alkyl, Ph; R1R2 = (CH2)4, CH2CH:CHCH:CHCH2, bond; R3 = H, halo, C1-6 alkyl, alkoxy; R4 = PhCH2, (un)substituted Ph, pyridinyl, pyrimidinyl, pyrazinyl; Z = SO2, SO2NR5; R5 = H, C1-6 alkyl; m = 0-4; n = 0-2] and their pharmaceutically acceptable salts were prepd. as antiinflammatories, e.g., by acylation of piperazines with arylsulfonyl chlorides. Thus, a soln. of 5-methoxyindan in MeCN was added dropwise over 0.5 h to a cooled and stirred soln. of ClSO3H, followed by heating 3 h at 50-60.degree.. The intermediate chlorosulfonated indan (II) in CH2Cl2 was treated with 1-(2-pyrimidinyl)piperazine dihydrochloride and Et3N, and stirred overnight to give I (R1, R2 = H, R3 = 6-MeO; Z = SO2; R4 = 2-pyrimidinyl, m, n = 0) which was converted to its hydrochloride. The latter at 50 mg/kg p.o. gave 55% inhibition of the acute inflammatory response in the rat carrageenan paw edema assay.

IT **125295-93-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and neutralization of, in prepn. of antiinflammatory)

RN 125295-93-4 CAPLUS

CN 1H-Indene-5-sulfonamide, 2,3-dihydro-6-methoxy-N-[2-[4-(2-pyrimidinyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



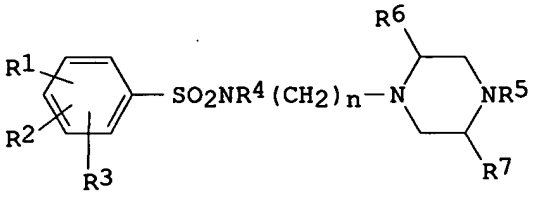
L8 ANSWER 74 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1990:98558 CAPLUS

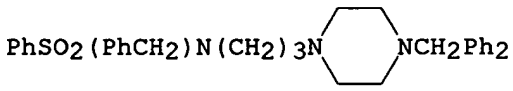
DN 112:98558
TI Preparation and testing of N-[(arylsulfamido)alkyl]piperazines as cardiovascular agents
IN Tanabe, Sohei; Sato, Seiichi; Kyotani, Yoshinori; Ohta, Tomio; Uchida, Kasumi
PA Kowa Co., Ltd., Japan
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI EP 330065 | A1 | 19890830 | EP 1989-102586 | 19890215 |
| EP 330065 | B1 | 19931110 | | |
| R: BE, CH, DE, FR, GB, IT, LI, NL, SE | | | | |
| JP 01211567 | A2 | 19890824 | JP 1988-33949 | 19880218 |
| JP 2556722 | B2 | 19961120 | | |
| US 4948892 | A | 19900814 | US 1989-310684 | 19890215 |
| PRAI JP 1988-33949 | A | 19880218 | | |

OS MARPAT 112:98558
GI

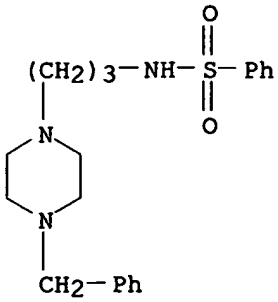



I




II

AB The title compds. [I; R1-R3 = H, halo, alkyl, alkoxy; R4 = H, alkyl, (substituted) aralkyl; R5 = (substituted) aryl, aralkyl; R6, R7 = H, alkyl, alkoxy; n = 1-8], useful as cardiovascular agents, were prepd. Thus, 1-diphenylmethyl-4-(3-aminopropyl)piperazine and Et3N in CH2Cl2 were treated with PhSO2Cl with ice cooling to give the sulfonamide which, in DMF, was treated with NaH and PhCH2Cl to give piperazine II. I inhibited 3,4-diaminopyridine-induced contraction of dog coronary artery rings at 10-6M. I also inhibited ADP-induced aggregation of rabbit platelet-rich plasma.
IT **125393-61-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiovascular agent)
RN 125393-61-5 CAPLUS
CN Benzenesulfonamide, N-[3-[4-(phenylmethyl)-1-piperazinyl]propyl]-, dihydrochloride (9CI) (CA INDEX NAME)

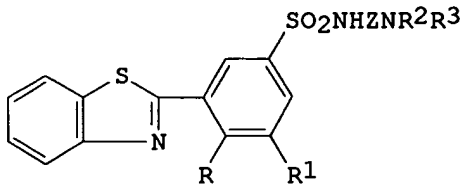


●2 HCl

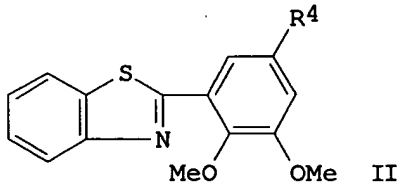
L8 ANSWER 75 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1986:478925 CAPLUS
DN 105:78925
TI Benzothiazolylbenzenesulfonamide derivatives
IN Hidaka, Hiroyoshi; Kawamatsu, Yutaka; Sugihara, Hirosada
PA Takeda Chemical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 61050975 | A2 | 19860313 | JP 1984-173922 | 19840820 |
| | JP 05022706 | B4 | 19930330 | | |
| PRAI | JP 1984-173922 | | 19840820 | | |

GI



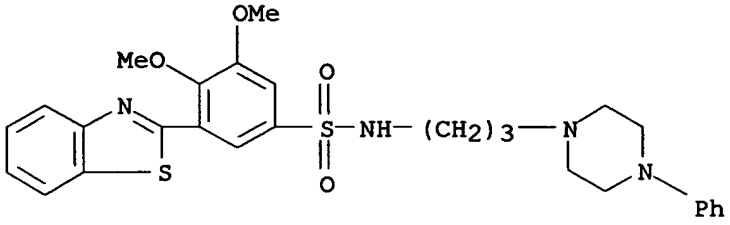
I



II

AB Title compds. I [R, R1 = H, lower alkoxy; R2, R3 = lower alkyl, (un)substituted aralkyl; NR2R3 = a ring; Z = alkylene] and their salts, useful as cerebro- and cardiovascular dilating agents, neoplasm inhibitors, and diarrhea inhibitors, were prepd. Thus, stirring 3.0 g phenylbenzothiazole deriv. II (R4 = H) with 9 mL ClSO3H at -20 to -10.degree. gave 3.6 g II (R4 = SO2Cl), which (2.0 g) was stirred with 1.3 g 3-(4-phenylpiperazinyl)propylamine in CHCl3 contg. 1.6 mL Et3N at room temp. for 2 h to give, after treatment with HCl, 1.6 g I-HCl [R = R1 = OMe, NR2R3 = 4-phenyl-1-piperazinyl, Z = (CH2)2], which dilated rabbit mesenteric artery in vitro (ED50 2.2 .mu.M).

IT **103625-76-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as cerebral and cardiovascular dilating agents, neoplasm inhibitors, and diarrhea inhibitors)
RN 103625-76-9 CAPLUS
CN Benzenesulfonamide, 3-(2-benzothiazolyl)-4,5-dimethoxy-N-[3-(4-phenyl-1-piperazinyl)propyl]-, hydrochloride (9CI) (CA INDEX NAME)

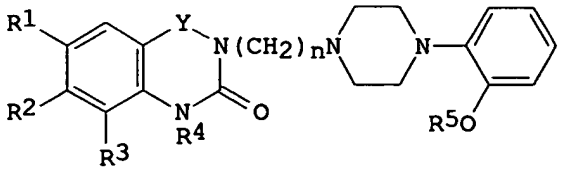



●x HCl

L8 ANSWER 76 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1986:148911 CAPLUS
DN 104:148911
TI Phenylpiperazine derivatives and their acid addition salts
IN Fukami, Harukazu; Kikumoto, Ryoji; Nakao, Kenichiro; Nitta, Issei; Inoue, Shinya
PA Mitsubishi Chemical Industries Co., Ltd., Japan
SO Eur. Pat. Appl., 56 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

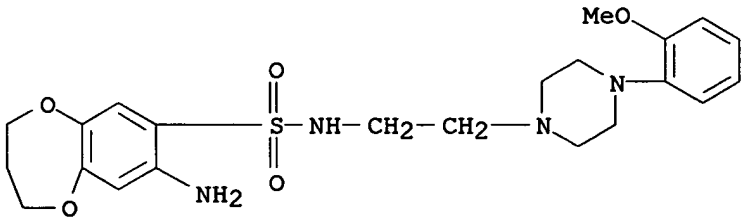
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 161498 | A1 | 19851121 | EP 1985-104477 | 19850412 |
| | EP 161498 | B1 | 19881012 | | |
| | R: BE, CH, DE, FR, GB, IT, LI, NL, SE | | | | |
| | JP 60222467 | A2 | 19851107 | JP 1984-77006 | 19840417 |
| | JP 05045586 | B4 | 19930709 | | |
| | JP 61083178 | A2 | 19860426 | JP 1984-203743 | 19840928 |
| | JP 05082388 | B4 | 19931118 | | |
| | JP 61087675 | A2 | 19860506 | JP 1984-209133 | 19841005 |
| | JP 05046341 | B4 | 19930713 | | |
| | JP 61161268 | A2 | 19860721 | JP 1985-1246 | 19850108 |
| | JP 05082386 | B4 | 19931118 | | |
| | US 4716161 | A | 19871229 | US 1985-719456 | 19850403 |
| | DK 8501619 | A | 19851018 | DK 1985-1619 | 19850410 |
| | DK 158518 | B | 19900528 | | |
| | DK 158518 | C | 19901105 | | |
| | HU 37615 | A2 | 19860123 | HU 1985-1384 | 19850415 |
| | HU 193361 | B | 19870928 | | |
| | CA 1287051 | A1 | 19910730 | CA 1985-479278 | 19850416 |
| PRAI | JP 1984-77006 | A | 19840417 | | |
| | JP 1984-203743 | A | 19840928 | | |

JP 1984-209133 A 19841005
JP 1985-1246 A 19850108
OS CASREACT 104:148911; MARPAT 104:148911
GI



I

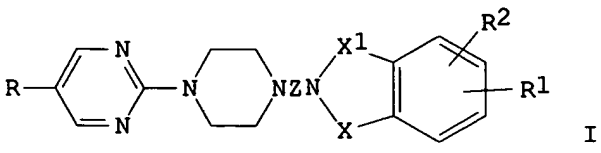
AB (Piperazinylalkyl)quinazolinediones and -benzothiadiazinones I [R1, R2 = H, alkoxy, NH2, AcNH, MeSO2NH, H2NCONH; R3 = H, alkoxy; R1R2, R2R3 = O(CH2)mO; R4,R5 = H, alkyl; Y = CO, S(O)2; n = 2-4; m = 1-3] were prepd. Thus, 6,7-dimethoxy-2,4(1H,3H)-quinazolinedione in DMF was treated with NaH and 1-(2-chloroethyl)-4-(2-methoxyphenyl)piperazine and stirred 6 h at 70.degree. to give 35% I (R1 = R2 = MeO, R3 = R4 = H, R5 = Me, Y = CO, n = 2) (II). In rats 3 mg II/kg orally reduced blood pressure 41.8%.
IT **101389-49-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclocondensation of, with trichloromethyl chloroformate)
RN 101389-49-5 CAPLUS
CN 2H-1,5-Benzodioxepin-7-sulfonamide, 8-amino-3,4-dihydro-N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 77 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1985:220896 CAPLUS
DN 102:220896
TI 2-Pyrimidinyl-1-piperazine derivatives and pharmaceuticals containing them
IN Dompert, Wolfgang; Glaser, Thomas; Horstmann, Harald; Schuurman, Teunis; Seidel, Peter Rudolf; Traber, Joerg
PA Troponwerke G.m.b.H. und Co. K.-G., Fed. Rep. Ger.
SO Ger. Offen., 121 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI DE 3321969 | A1 | 19841220 | DE 1983-3321969 | 19830618 |

| | | | | | |
|---|---|---|---|---|---|
| | EP 129128 | A2 | 19841227 | EP 1984-106336 | 19840604 |
| | EP 129128 | A3 | 19850522 | | |
| | EP 129128 | B1 | 19901122 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | AT 58534 | E | 19901215 | AT 1984-106336 | 19840604 |
| | AU 8429293 | A1 | 19841220 | AU 1984-29293 | 19840612 |
| | AU 569086 | B2 | 19880121 | | |
| | ES 533338 | A1 | 19850801 | ES 1984-533338 | 19840612 |
| | FI 8402419 | A | 19841219 | FI 1984-2419 | 19840614 |
| | FI 82936 | B | 19910131 | | |
| | FI 82936 | C | 19910510 | | |
| | DK 8402959 | A | 19841219 | DK 1984-2959 | 19840615 |
| | DK 165447 | B | 19921130 | | |
| | DK 165447 | C | 19930413 | | |
| | HU 34746 | O | 19850429 | HU 1984-2325 | 19840615 |
| | HU 196391 | B | 19881128 | | |
| | IL 72120 | A1 | 19890928 | IL 1984-72120 | 19840615 |
| | CA 1300624 | A1 | 19920512 | CA 1984-456741 | 19840615 |
| | JP 60023373 | A2 | 19850205 | JP 1984-123884 | 19840618 |
| | JP 06060165 | B4 | 19940810 | | |
| | ZA 8404585 | A | 19850227 | ZA 1984-4585 | 19840618 |
| | ES 542320 | A1 | 19851216 | ES 1985-542320 | 19850416 |
| | ES 542321 | A1 | 19851216 | ES 1985-542321 | 19850416 |
| | ES 542322 | A1 | 19851216 | ES 1985-542322 | 19850416 |
| | ES 542323 | A1 | 19851216 | ES 1985-542323 | 19850416 |
| | ES 542319 | A1 | 19860601 | ES 1985-542319 | 19850416 |
| | US 4818756 | A | 19890404 | US 1986-838238 | 19860310 |
| | US 4937343 | A | 19900626 | US 1988-247813 | 19880922 |
| | US 4988809 | A | 19910129 | US 1990-482580 | 19900221 |
| | US 5187276 | A | 19930216 | US 1990-619270 | 19901128 |
| | DK 9200310 | A | 19920306 | DK 1992-310 | 19920306 |
| | DK 168740 | B1 | 19940530 | | |
| | US 5314884 | A | 19940524 | US 1992-938187 | 19920831 |
| PRAI | DE 1983-3321969 | A | 19830618 | | |
| | EP 1984-106336 | A | 19840604 | | |
| | US 1984-617858 | A3 | 19840606 | | |
| | US 1986-838238 | A3 | 19860310 | | |
| | US 1988-247813 | A3 | 19880922 | | |
| | US 1990-482580 | A3 | 19900221 | | |
| | US 1990-619270 | A3 | 19901128 | | |
| OS | CASREACT 102:220896 | | | | |
| GI | | | | | |




I

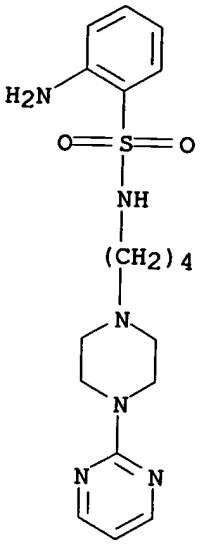
AB The title compds. [I; R = H, halo, OH, NO2, cyano, amino, alkylthio aralkyl, (un)substituted alkyl, aryl, heteroaryl, alkoxy; R1, R2 = H, aralkyl, cycloalkyl, PhO, halo, OH, NO2, alkylthio, PhS, cyano, CO2H alkoxycarbonyl, carbamoyl, sulfamoyl, (un)substituted alkyl, aryl, alkoxy; X = CO, SO2, COCH2, CONR3; R3 = H, (un)substituted alkyl, aryl; X1 = CO, SO2] were prepd. Thus, (N-(4-bromobutyl)phthalimide was stirred under N

at 120-130.degree. with 1-(2-pyrimidinyl)piperazine to give 96% I (R-R2 = H, X = X1 = CO). Selected I are antidepressants, inhibiting tetrabenazine-induced ptosis in mice with an ED50 of 5-40 mg/kg i.p.

IT **95847-25-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclocondensation of, with phosgene)

RN 95847-25-9 CAPLUS

CN Benzenesulfonamide, 2-amino-N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-(9CI) (CA INDEX NAME)



L8 ANSWER 78 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1984:490978 CAPLUS

DN 101:90978

TI Piperazine derivatives

PA Sumitomo Chemical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF

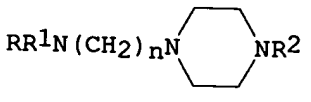
DT Patent

LA Japanese

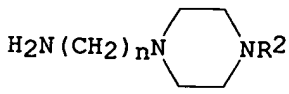
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 59029665 | A2 | 19840216 | JP 1982-140297 | 19820811 |
| PRAI | JP 1982-140297 | | 19820811 | | |

GI



I



II

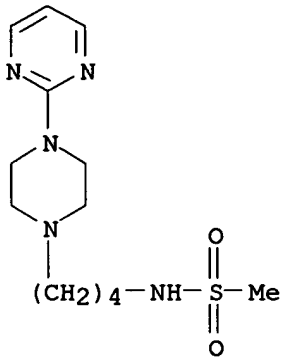
AB Twenty-one piperazine derivs. I [R = R3Z; R1 = H, R4Z1 (R3, R4 = alkyl,

aryl, alkoxy, PhO, PhCH2O, H, NH2; Z, Z1 = SO2, CO); n = 2-4; R2 = 2-pyridyl, 2-pyrimidinyl] were prepd. by, e.g., reaction of R5ZX (R5 = alkyl, aryl, alkoxy, PhO, PhCH2O, X = halo) with II. I has antianxiety activity (no data). Thus, 692 mg ClCO2Et in Et2O was added to a mixt. of 1 g II (n = 4, R2 = 2-pyrimidinyl) and 680 mg Et3N in Et2O-THF with ice cooling and the mixt. kept at 4.degree. to give 38.5% I.cntdot.HCl (R = EtO2C, R1 = H, n = 4, R2 = 2-pyrimidinyl).

IT **91517-07-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 91517-07-6 CAPLUS

CN Methanesulfonamide, N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L8 ANSWER 79 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1984:6557 CAPLUS

DN 100:6557

TI 1-Phenylpiperazine derivatives having antiaggressive activity

IN Van Dalen-Van der Aa, Dirkje A.; Hulkenberg, Antonius

PA Duphar International Research B. V., Neth.

SO Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW

DT Patent

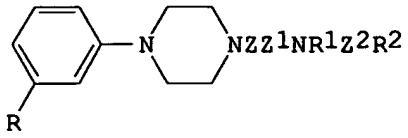
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 89089 | A1 | 19830921 | EP 1983-200346 | 19830311 |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | DK 8301016 | A | 19830913 | DK 1983-1016 | 19830228 |
| | ES 520439 | A1 | 19840416 | ES 1983-520439 | 19830309 |
| | ZA 8301625 | A | 19841031 | ZA 1983-1625 | 19830309 |
| | AU 8312334 | A1 | 19830915 | AU 1983-12334 | 19830310 |
| | JP 58180478 | A2 | 19831021 | JP 1983-38414 | 19830310 |
| PRAI | NL 1982-1032 | A | 19820312 | | |

OS MARPAT 100:6557

GI



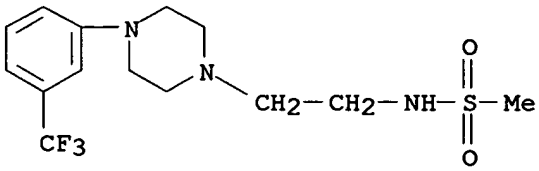

I

AB Piperazines I (R = CF3, Cl; Z = CH2, CH2CH2, CHMeCH2, CH2CHMe; Z1 = CH2, CO, SO2; R1 = H, Me, Et; Z2 = CO, SO2; R2 = NH2, alkylamino, dialkylamino, alkyl, cyclohexyl, cyclohexylmethyl, cyclohexyloxymethyl, benzyl, thenyl, pyridylmethyl, PhOCH2, PhSCH2, a 1-phenylcycloalkyl group, alkoxy, cycloalkyloxy, aralkoxy), useful as anti-aggressive agents (no data), were prepd. Thus, a mixt. of ClCH2CH2CONHSO2NH2, 1-[3-(trifluoromethyl)phenyl]piperazine, and Et3N in THF was refluxed to give I (R = CF3, Z = CH2CH2, Z1 = CO, R1 = H, Z2 = SO2, R2 = NH2).

IT **88069-02-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 88069-02-7 CAPLUS

CN Methanesulfonamide, N-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)




L8 ANSWER 80 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1981:424983 CAPLUS

DN 95:24983

TI Synthesis of N-(3-amino-2-hydroxy propyl)-N-sulfonylanilines derivatives. Potential antianginal activities

AU Goldenberg, Charles; Van Meerbeeck, Clement; Wandestrick, Raymond; Descamps, Marcel; Tornay, Chantal; Dirks, Michel; Colot, Michel; De Claviere, Michel

CS Cent. Rech. S.A., Labaz N.V., Brussels, B-1120, Belg.

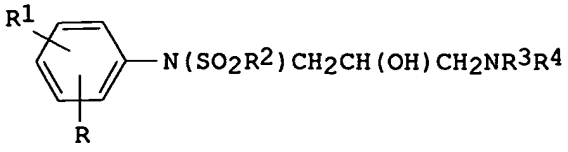
SO European Journal of Medicinal Chemistry (1980), 15(6), 545-50
CODEN: EJMCA5; ISSN: 0009-4374

DT Journal

LA French

OS CASREACT 95:24983

GI



I

AB The title compds. I [R = 2-allyloxy, 4-AcNH, 4-H2NCOCH2, R1 = H; R = 2-Cl, R1 = 6-Cl; R = 3-Cl, R1 = 4-Cl; R2 = Me, 4-MeC6H4, 4-MeOC6H4, Ph; R3 = H, R4 = CHMe2, CMe3, CH2CH2OPh, (CH2)3Ph; NR3R4 = pyrrolidino, morpholino, 4-substituted piperazino] were prepd. by sulfonylating RR1C6H3NH2, treating RR1C6H3NHSO2R2 with epichlorohydrin, and aminolysis. I have both .alpha.- and .beta.-sympatholytic activity.

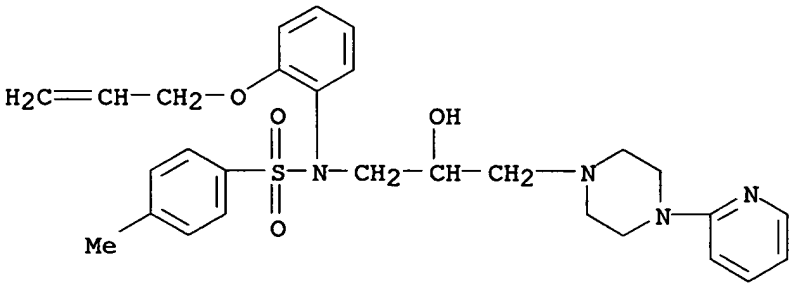
IT **77166-16-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and sympatholytic activity of)

RN 77166-16-6 CAPLUS

CN Benzenesulfonamide, N-[2-hydroxy-3-[4-(2-pyridinyl)-1-piperazinyl]propyl]-4-methyl-N-[2-(2-propenyloxy)phenyl]-, ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

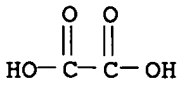
CM 1

CRN 77166-15-5
CMF C28 H34 N4 O4 S



CM 2

CRN 144-62-7
CMF C2 H2 O4

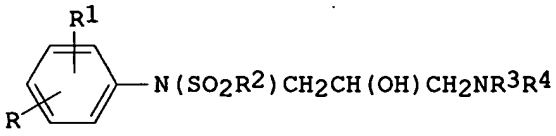


L8 ANSWER 81 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1981:191892 CAPLUS

DN 94:191892
TI Sulfonyl aniline derivatives and their use in therapy
IN Descamps, Marcel; Goldenberg, Charles
PA Omnium Financier Aquitaine pour l'Hygiene et la Sante, Fr.
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 22118 | A1 | 19810107 | EP 1980-870033 | 19800610 |
| | EP 22118 | B1 | 19830601 | | |
| | R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| | FR 2459235 | A1 | 19810109 | FR 1979-15232 | 19790614 |
| | FR 2459235 | B1 | 19820917 | | |
| | US 4330542 | A | 19820518 | US 1980-150411 | 19800516 |
| | AT 3638 | E | 19830615 | AT 1980-870033 | 19800610 |
| | JP 56032450 | A2 | 19810401 | JP 1980-80825 | 19800613 |
| PRAI | FR 1979-15232 | A | 19790614 | | |
| | EP 1980-870033 | A | 19800610 | | |

OS CASREACT 94:191892
GI




I

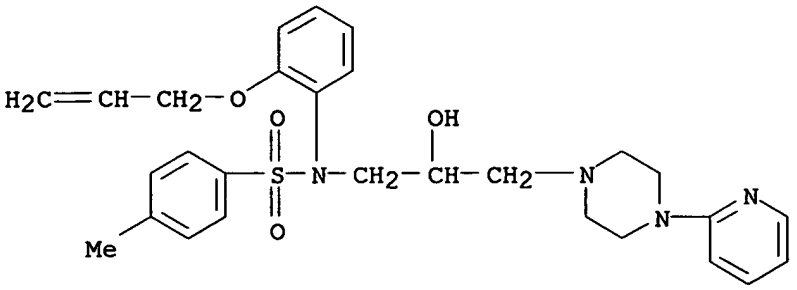
AB N-Glycidyl-N-sulfonylanilines were treated with amines to yield the resp. N-(3-amino-2-hydroxypropyl)anilines I [R ,R1 (same or different) = CH2:CHCH2O, AcNH, carbamoyl, H, Cl; R2 = Me, Ph, methyl- or methoxyphenyl; R3 = H ; R4 = CHMe2, CMe3, CH2CH2OPh, (CH2)3Ph; or NR3R4 = pyrrolidino, morpholino, 4-substituted 1-piperazinyl], useful in the treatment of angina pectoris (no data). 2-Allyloxy-N-glycidyl-N-mesylaniline was heated with Me2CHNH2 in EtOH to give I (R = 2-CH2:CHCH2O, R2 = Me, R4 = CHMe2, R1 = R3 = H).

IT **77166-16-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 77166-16-6 CAPLUS
CN Benzenesulfonamide, N-[2-hydroxy-3-[4-(2-pyridinyl)-1-piperazinyl]propyl]-4-methyl-N-[2-(2-propenyloxy)phenyl]-, ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

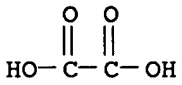
CM 1

CRN 77166-15-5
CMF C28 H34 N4 O4 S

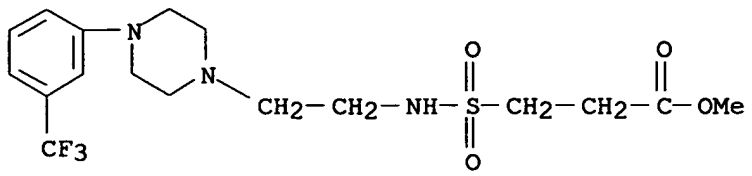


CM 2

CRN 144-62-7
CMF C2 H2 O4



L8 ANSWER 82 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1977:495439 CAPLUS
DN 87:95439
TI Substituted trifluoromethyl phenyl piperazines as anorectic agents
AU Cross, Peter E.; Dickinson, Roger P.; Halliwell, Geoffrey; Kemp, John E. G.
CS Pfizer Cent. Res., Pfizer Ltd., Sandwich/Kent, UK
SO European Journal of Medicinal Chemistry (1977), 12(2), 173-6
CODEN: EJMCA5; ISSN: 0223-5234
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB In a series of trifluoromethyl phenyl piperazines possessing cyclo-imido alkyl side chains (I) several compds. possessed good anorectic activity with min. side effects on the central nervous system. The most potent no. of the series was 1-(2-succinimidoethyl)-4-[4'-chloro-3-trifluoromethyl)phenyl]piperazine-HCl (II) [41213-05-2], which was prepd. by heating 1-[4'-chloro-3-(triffluoromethyl)phenyl]piperazine-HCl [63556-37-6] with 2-succinimidoethyl chloride [41212-96-8] in dry dimethylformamide in the presence of base.
IT **63556-39-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 63556-39-8 CAPLUS
CN Propanoic acid, 3-[[[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]amino]sulfonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

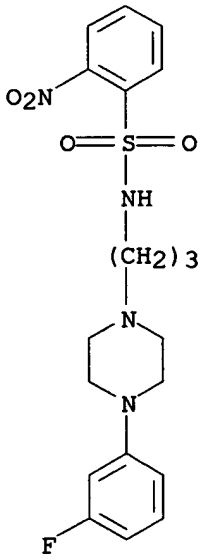
L8 ANSWER 83 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1969:87765 CAPLUS
DN 70:87765
TI Sedative, antiadrenergic, and hypotensive 2-substituted 2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxides
AU Hayao, Shin; Strycker, W. G.; Phillips, B. M.; Fujimori, H.; Vidrio, H.
CS Ther. Res. Div., Miles Lab., Inc., Elkhart, IN, USA
SO Journal of Medicinal Chemistry (1968), 11, 1246-8
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB Treatment of o-nitro-benzenesulfonyl chloride with amines gave o-nitrobenzenesulfon-amides which were hydrogenated to o-aminobenzenesulfonamides which were cyclized by treatment with COCl2 in boiling PhCl to give 2-substituted 2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxides. Similarly, o-aminobenzenesulfonamide was cyclized with urea at 200.degree. or with COCl2 in boiling PhCl to give unsubstituted 2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide, which was alkylated to give 2-substituted compds. An ice-cold soln. of 55 g. 1-(3-aminopropyl)-4-(m-fluorophenyl)piperazine in 150 ml. C6H6 and 100 ml. 20% NaOH soln. was treated with a soln. of 51.3 g. o-nitrobenzenesulfonyl chloride in 150 ml. C6H6 and the reaction mixt. stirred 2 hrs. at 25.degree., acidified with dil. HCl, and made basic with NH4OH to give 78.8 g 4-(m-fluorophenyl)-1-[3-(o-nitrobenzenesulfonamido)propyl]piperazin e (I) m. 111-12.degree. (C6H6-hexane). A soln. of 77.5 g. I in 210 ml. HOAc was hydrogenated over 5 g. 10% Pd/C to give 65.2 g. 1-[3-(o-amino-benzenesulfonamido)propyl]-4-(m-fluorophenyl)piperazine (II), m. 119-20.degree. (C6H6-hexane and MeOH). To an ice-cold soln. of 250 ml. PhCl contg. 50.9 g. COCl2 was added 44.4 g. II and the suspension refluxed 1 hr. to give 39.0 g. 2-[3-(4-m-fluorophenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide (III) hydrochloride, m. 257-8.degree. (decompn.) (MeOH- HCONMe2). The combined filtrates were concd. in vacuo and made basic with NH4OH to give 12.4 g. III, m. 148-9.degree. (MeOH). A soln. of 34.1 g. 6-chloro-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide and 23.8 g. NaOMe in 200 ml. abs. EtOH and 100 ml. Me2SO was treated with 45.4 g. 1-(3-chloropropyl)-4-phenylpiperazine dihydrochloride and refluxed 20 hrs. The soln. was filtered and the filtrate concd. in vacuo and worked up to give 14.0 g. 6-chloro-2-[3-(4-phenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide hydrochloride (IV), m. 227-9.degree. (decompn.); free base m. 152-3.degree. (aq. MeOH-HCONMe2). V prepd. were (n, Q, m.p., and m.p. HCl salt given): 3, 4-phenyl-1-piperazinyl, 152-3.degree., 256-7.degree. (decompn.); 3, 4-(m-chlorophenyl)-1-piperazinyl,

149-50.degree., 224-6.degree. (decompn.); 3, 4-(m-trifluoromethylphenyl)-1-piperazinyl, 158-9.degree., 262-3.degree. (decompn.); 3, 4-(p-fluorophenyl)-1-piperazinyl, 165-7.degree., 228-30.degree.; 3, 4-phenyl-1-piperidinyl, 161-2.degree., 219-20.degree. (decompn.); 4, 4-(m-chlorophenyl)-1-piperazinyl, 161-3.degree. (decompn.), -; 5, 4-phenyl-1-piperazinyl, 190.degree. (decompn.), -. In exptl. animals, the activity of 2-[3-(4-p-fluorophenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiodiazin-3(4H)-one 1,1-dioxide hydrochloride (VI) as a psychosedative was comparable to that of chlorpromazine and 3-[3-(4-m-chlorophenyl-1-piperazinyl)propyl]-2,4(1H,3H)-quinazolinedione hydrochloride. Except for VI, the compds. showed weaker sedative and hypotensive activities than the corresponding 3-substituted 2,4(1H,3H)-quinazolinediones. Studies of the antiadrenergic and hypotensive activities indicated that the unsubstituted phenylpiperazine and phenylpiperidine derivs. had greater activity than compns. with substituents in the Ph ring. The compds. produced a small decrease in the water and electrolyte excretion in rats.

IT **21920-27-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 21920-27-4 CAPLUS

CN Benzenesulfonamide, N-[3-[4-(m-fluorophenyl)-1-piperazinyl]propyl]-o-nitro- (8CI) (CA INDEX NAME)



L8 ANSWER 84 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1967:10968 CAPLUS

DN 66:10968

TI 2H-1,2,4-Benzothiadiazine-3(4H)-one 1,1-dioxide derivatives

IN Hayao, Shin

PA Miles Laboratories, Inc.

SO U.S., 6 pp.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

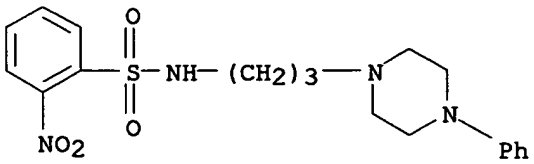
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 3267096 | | 19660816 | US | 19650224 |

GI For diagram(s), see printed CA Issue.

AB The title compds. are useful as central as central nervous system depressants, antiinflammatory agents, and antihypertensive agents and were prepd. according to the given scheme (n = 3 to 5 and X is H F, Cl, or F3C). Thus, to an ice cold soln. of 43.8 1-(3-aminopropyl)-4-phenylpiperazine in 100 ml. C6H6 and 100 ml. 20% NaOH was added with vigorous stirring a soln. of 44.3 g. o-O2NC6H4SO2Cl in 100 ml. C6H6. The brown cloudy soln. was stirred an hr. and acidified with dil. HCl soln. to give a gummy mixt., which was made basic with NH4OH to give a light yellow solid. After filtration, the solid was washed with H2O and Et2O and dried at 50.degree. to give 98% N-[3-(4-phenyl-1-piperazinyl)-propyl]-2-nitrobenzenesulfonamide (I), m. 175.degree. (softens at 135.degree.); recrystd. product m. 138-9.degree. [aq. MeOH-HCONMe2 (DMF)], yield 24.9 g. A soln. of 23.9 g. I in 200 ml. HOAc was reduced over 5 g. freshly prepd. 5% Pd-C with shaking overnight. The mixt. was filtered, the solvent removed, the residual sirup cooled in an ice-H2O bath, and basified with concd. NH4OH soln., and the gracy oil taken into CHCl3-Et2O and dried over MgSO4. A satd. soln. of HCl in iso-PrOH, (200 ml.) was added and the product isolated (24.9 g.) was the HCl salt of 2-amino-N-[3-(4-phenyl-1-piperazinyl)propyl]benzenesulfonamide, m. 226-8.degree.; the free base (II), m. 117-18.degree.. A slow stream of COCl2 was bubbled 60 min. into a boiling soln. of 31.3 g. II in 250 ml. ClPh, the mixt. cooled, and the solid product collected, washed with EtOAc-Et2O and H2O, and air-dried to give 38.2 g. product, m. 226-32.degree.. The product was titurated with aq. NH4OH to yield 35.2 g. 2-[3-4(-phenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiazin-3(4H)-one 1,1-dioxide (III), m. 151-4.degree. (aq. Me2CO). III was dissolved in hot MeOH satd. with HCl to give 26.6 g. III.HCl.-MeOH, m. 256-7.degree.. By a similar sequence of reactions, 76.1 g. 2-nitro-N-[3-(4-m-chlorophenyl-1-piperazinyl)propyl]benzenesulfonamide gave 75.8 g. 2-amino-N-[3-(4-m-chlorophenyl-1-piperazinyl)propyl]benzenesulfonamide-HCl.MeOH (IV), m. 155-6.degree. (decompn.) (methanolic HCl-EtOAc). The HCl salt was suspended in H2O, aq. NH4OH added, the orange-yellow gum extd. with CHCl3 to yield 54.8 g. of the free base of IV, m. 105-7.degree.. Reaction with COCl2 in ClPh gave 47.4 g. 2-[3-(4-m-chlorophenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiazin-3(4H)-one 1,1-dioxide-HCl (V), m. 224-6.degree. (aq. MeOH-DMF). The free base of V (9.5 g.), m. 149-50.degree., was isolated from the filtrate. Likewise, 44 g. 1-m-chlorophenyl-4-(4-aminobutyl)piperazine was converted to 2-nitro-N-[4-m-chlorophenyl-1-piperazinyl)butyl]benzene sulfonamide. Redn. yielded 67.6 g. of the HCl salt of 2-amino-N-[4-(4-m-chlorophenyl-1-piperazinyl)butyl]benzenesulfonamide which is converted to the free base on treatment with aq. NH4OH. The free base (51.4 g.) was allowed to react with COCl2 to give 44.9 g. 2-[4-(4-m-chlorophenyl-1-piperazinyl)butyl]-2H-1,2,4-benzothiazin-3(4H)-one 1,1-dioxide-HCl (VI), m. 210-16.degree. (decompn.), which on treatment with aq. NH4OH yielded 29.1 g. the free base of VI, m. 133-4.degree., and this base was converted to 33.1 g. of the maleic acid salt, m. 161-3.degree. (decompn.) (EtOAc). The reaction of COCl2 in ClPh with 76 g. 2-amino-N-[3-(4-m-trifluoromethylphenyl-1-piperazinyl)propyl]benzenesulfonamide gave a product which was dissolved in Et2O and treated with maleic acid to give 91.7 g., m. 173-83.degree. (decompn.), of a crude maleate. It was converted to the free base to give 45 g. 2-[3-(4-m-trifluoro-methylphenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide (VII), m. 141-53.degree. (aq. MeOH). The VII obtained and maleic acid in MeOH gave 28.4 g. VII.C4H4O4, m.

184-5.degree. (MeOH-Et2O), and was converted to 10.7 g. VII.HCl, m. 262-3.degree. (decompn.). 1-(Aminopropyl)-4-phenylpiperidine (40.1 g.) was converted to 59.4 g. 2-nitro-N-[3-(4-phenyl-1-piperidinyl)propyl]benzenesulfonamide (VIII), m. 113-14.degree. (aq. MeOH). Redn. of the nitro group in VIII to an amino group, followed by the treatment with COCl2 in ClC6H5 gave 20.8 g. 2-[3-(4-phenyl-1-piperidinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide-HCl.MeOH (IX), m. 219-20.degree. (aq. MeOH). Addn. of aq. NH4OH to the filtrates of the crystn. liquors gave 16 g. of the free base of IX, m. 161-2.degree. (aq. Me2CO). 2-Nitro-N-[5-(4-phenyl-1-piperazinyl)pentyl]benzenesulfonamide (X) (77%), m. 128-30.degree. (aq. MeOH-DMF), was obtained from 1-(5-aminopentyl)-4-phenylpiperazine. Redn. of 74.3 g. X with H in the presence of Pd-C gave 54.2 g. 2-amino-N-[5-(4-phenyl-1-piperazinyl)pentyl]benzenesulfonamide, m. 152-3.degree. (Me2CO-CHCl3-n-C6H14), of which 52.9 g. was converted to 22.2 g. 2-[5-(4-phenyl-1-piperazinyl)pentyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide-2HCl, m. 190.degree. (decompd. 175.degree.) (MeOH contg. HCl). 1-(3-Aminopropyl)-4-fluorophenylpiperazine (35.6 g.) gave 40.3 g. 2-nitro-N-[3-(4-p-fluorophenyl-1-piperazinyl)propyl]benzenesulfonamide, m. 132-3.degree. (Me2CO-MeOH-n-C6H14), of which 39 g. was reduced to yield 34.2 g. of 2-amino-N-[3-(4-p-fluorophenyl)propyl]benzenesulfonamide, m. 121-2.degree. (aq. MeOH), and 40 g. of this compd. was treated with COCl2 to yield 30.2 g. of 2-[3-(4-p-fluorophenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide-HCl, m. 228-230.degree. (aq. MeOH-EtOAc). Spectral data are included in the analytical results for the new compds.

IT **13349-02-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 13349-02-5 CAPLUS
CN Benzenesulfonamide, o-nitro-N-[3-(4-phenyl-1-piperazinyl)propyl]- (8CI) (CA INDEX NAME)

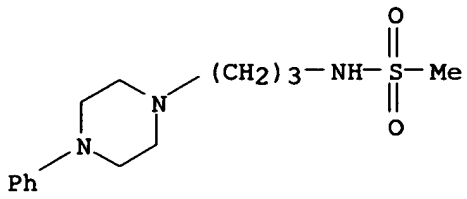



L8 ANSWER 85 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1956:32338 CAPLUS
DN 50:32338
OREF 50:6522c-d
TI Phenyl-substituted piperazine compounds
IN Fleming, Robert W.; Parcell, Robert F.
PA Parke, Davis & Co.
DT Patent
LA Unavailable
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2722529 | | 19551101 | US | |

AB See Brit. 721,417 (C.A. 50, 2683i).
IT **500797-20-6**, Methanesulfonamide, N-[3-(4-phenyl-1-

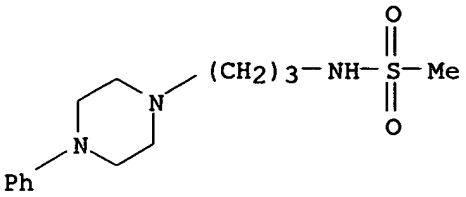
piperazinyl)propyl]-
(prepn. of)
RN 500797-20-6 CAPLUS
CN Methanesulfonamide, N-[3-(4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 86 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1956:12597 CAPLUS
DN 50:12597
OREF 50:2683i,2684a-b
TI Phenyl substituted piperazine compounds
PA Parke, Davis & Co.
DT Patent
LA Unavailable
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 721417 | | 19550105 | GB | |

GI For diagram(s), see printed CA Issue.
AB In this abstr. R = CH2.CH2.NPh.CH2.CH2.N. RCH2CH2CH2NH2 (21.9 g.) and 100 cc. EtO2CH is heated under reflux for 2 h., the excess ester removed by distn. and the residue recrystd. from C6H6 and petr. ether to yield 8 g. RCH2CH2CH2NHCOH, m. 100-1.degree.. The following compds. are also described: RCH2CH2CH2NHCOCHCl2, m. 81-2.degree.; RCH2CH2CH2NHSO2Me (I), m. 105-7.degree.; I.HBr salt, m. 172-4.degree.; RCH2CH2CH2NHBz, m. 109-10.degree.; R(CH2)6NHCOH, m. 65-7.degree.; R(CH2)3NHAc, m. 100-2.degree.; R(CH2)3NHCONH2, m. 146-8.degree.; RCH2CHMeNHAc, m. 96-8.degree.; R(CH2)3NHCOR' (R' = cyclohexyl), m. 112-14.degree.; R(CH2)3NHCO(CH2)5R', m. 90-1.degree.; R(CH2)2NHCOCH2Ph, m. 127-9.degree.; RCH2CH2NHCOH, m. 95-6.degree.; RCH2CH2NHAc, m. 105-7.degree.; R(CH2)3NHCOEt, m. 81-2.degree.; R(CH2)4NHtAc, m. 107-8.degree.; R(CH2)5NHAc, m. 86-7.degree.; R(CH2)4NHSO2Me, m. 80-1.degree.; R(CH2)5NHSO2Me, m. 103-5.degree..
IT **500797-20-6**, Methanesulfonamide, N-[3-(4-phenyl-1-piperazinyl)propyl]-
(prepn. of)
RN 500797-20-6 CAPLUS
CN Methanesulfonamide, N-[3-(4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



```
=> file caold
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       440.38     625.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                       -64.50     -64.50

FILE 'CAOLD' ENTERED AT 19:36:23 ON 27 JAN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.  Title keywords, authors, patent
  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

  New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file supports REGlstRY for direct browsing and searching of
  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.

=> s l5
L9             0 L5

=> log h
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         1.76     627.50

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                         0.00     -64.50

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 19:38:44 ON 27 JAN 2006
```

| | ENTRY | SESSION |
|---|---|---|
| FULL ESTIMATED COST | 11.44 | 11.65 |

FILE 'CAPLUS' ENTERED AT 15:16:15 ON 29 JAN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 29 Jan 2006 VOL 144 ISS 6
FILE LAST UPDATED: 27 Jan 2006 (20060127/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

```
=> s l2
L3          86 L2

=> d l3 11 19 29 34 40-42 53 60 63 67 74 79 83-86 bib abs hitstr
```

L3 ANSWER 11 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:675719 CAPLUS
DN 141:207226
TI Preparation of arylpiperazinyl sulfonamides as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating CND disorders, especially anxiety and related diseases
IN Dhanoa, Dale S.; Chen, Dongli; Becker, Oren; Noiman, Silvia; Cheruku, Srinivasa Rao; Marantz, Yael; Sharadendu, Anurag; Shachem, Sharon; Heifetz, Alexander; Mohanty, Pradyumna; Inbal, Boaz; Fichman, Merav; Nudelman, Raphael; Bar-Haim, Shay
PA Predix Pharmaceuticals Holdings, Inc., USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2004069794 | A2 | 20040819 | WO 2004-US2858 | 20040202 |
| | WO 2004069794 | A3 | 20041104 | | |
| | WO 2004069794 | C2 | 20041209 | | |
| | WO 2004069794 | B1 | 20050127 | | |

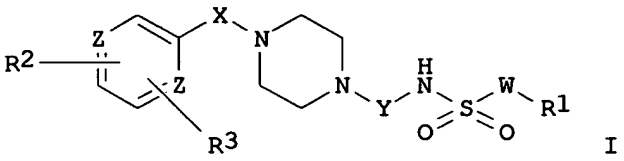
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

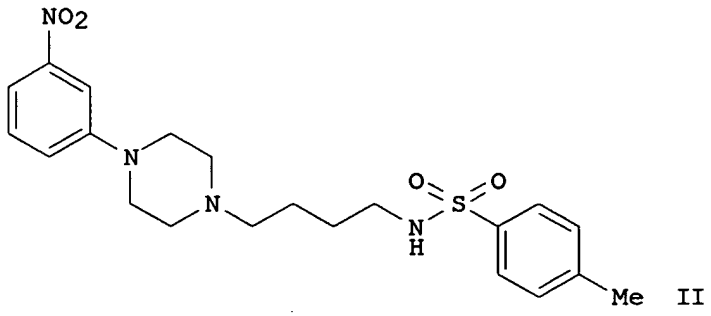
| | | | | | |
|---|---|---|---|---|---|
| US 2004220192 | A1 | 20041104 | US 2004-768579 | | 20040130 |
| CA 2513915 | AA | 20040819 | CA 2004-2513915 | | 20040202 |
| EP 1592425 | A2 | 20051109 | EP 2004-707409 | | 20040202 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| PRAI US 2003-443988P | P | 20030131 | | | |
| US 2003-458297P | P | 20030328 | | | |
| US 2003-503520P | P | 20030916 | | | |
| US 2004-768579 | A2 | 20040130 | | | |
| WO 2004-US2858 | W | 20040202 | | | |

OS MARPAT 141:207226

GI



I

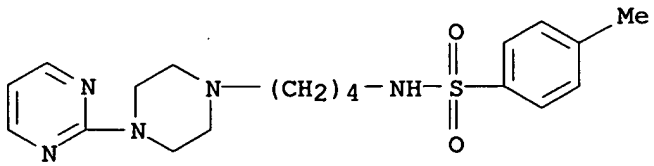


II

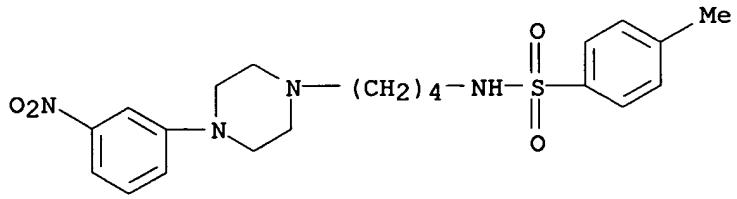
AB Title compds. I [wherein R1 = (un)substituted alkyl-aryl, cyclo/alkyl; R2, R3 = independently H, lower alkyl, cycloalkyl, trihalomethyl, halo, etc.; Z = N or C; X = (CH2)m; m = 0-6; Y = (CH2)n; n = 1-6; W = (CH2)p; p = 0-4; N together with one or several carbons from Y = 4-, 5-, 6- or 7-membered hetero/cyclic ring; their pharmaceutically acceptable salts and/or esters, and provided that when p=o, R1 is not (un)substituted aryl and R2, R3 are independently other than alkoxy/phenyl] were prepd. as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating anxiety and related disorders. Three biol. examples are given. For example, II.bul.2HCl was prepd., in 3 steps, from 1-amino-4-butanol, tosyl chloride, 1-(3-nitrophenyl)piperazine, and HCl. Selected I bound to 5-HT1A receptor with Ki values in the 1.3 - 26 nM range. Thus, I are useful for treating central nervous system disorders such as generalized anxiety disorder, ADD/ADHD, neural injury, stroke, and migraine.

IT **690949-14-5P**, 4-Methyl-N-[4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl]benzenesulfonamide **740872-80-4P**, 4-Methyl-N-[4-[4-(3-nitrophenyl)piperazin-1-yl]butyl]benzenesulfonamide **740872-83-7P**, Cyclopropanecarboxylic acid N-[3-[4-[4-[(4-tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]amide **740872-88-2P**, N-[3-[4-[4-[(4-Tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide **740872-96-2P**, 4-Methyl-N-[4-[4-(pyridin-2-yl)piperazin-1-yl]butyl]benzenesulfonamide **740873-08-9P**, Cyclopropanecarboxylic acid N-[3-[4-[4-[(cyclohexylmethylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]amide **740873-12-5P**, N-[3-[4-[4-[(Propan-2-ylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide **740873-15-8P**, N-[3-[4-[4-[(2-Methylpropan-1-ylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide **740873-18-1P**, N-[3-[4-[4-[(Cyclohexylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide **740873-25-0P**, N-[3-[4-[4-[(Cyclohexylmethylsulfonyl)(methyl)amino]butyl]piperazin-1-yl]phenyl]acetamide **740873-29-4P** **740873-33-0P**, 1-Cyclohexyl-N-[4-[4-(2-methoxyphenyl)piperazin-1-yl]butyl]methanesulfonamide **740873-36-3P**, 1-Cyclohexyl-N-[4-[4-(3-dimethylaminophenyl)piperazin-1-yl]butyl]methanesulfonamide **740873-40-9P**, 1-Cyclohexyl-N-[4-[4-(pyridin-2-yl)piperazin-1-yl]butyl]methanesulfonamide **740873-55-6P**, N-[3-[4-[4-[(4-Fluorobenzenesulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(5-HT1 agonist; prepn. of arylpiperazinyl sulfonamides as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating anxiety and related disorders)

RN 690949-14-5 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-(9CI) (CA INDEX NAME)

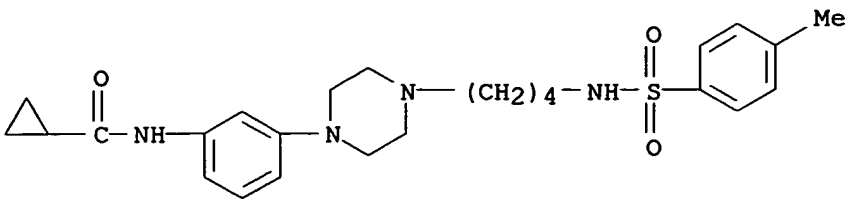



RN 740872-80-4 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(3-nitrophenyl)-1-piperazinyl]butyl]-(9CI) (CA INDEX NAME)

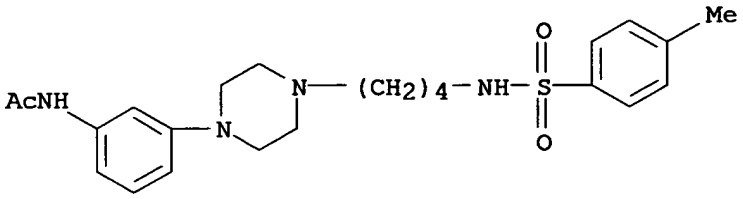



RN 740872-83-7 CAPLUS
CN Cyclopropanecarboxamide, N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl

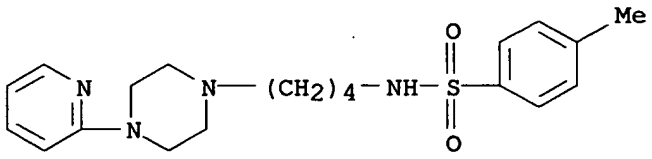
]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



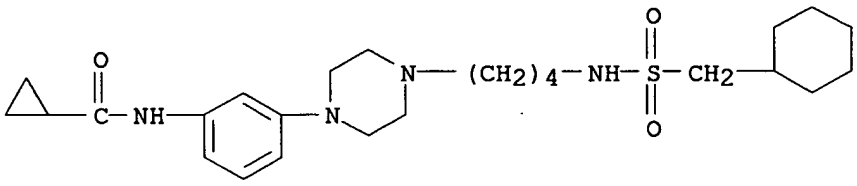
RN 740872-88-2 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



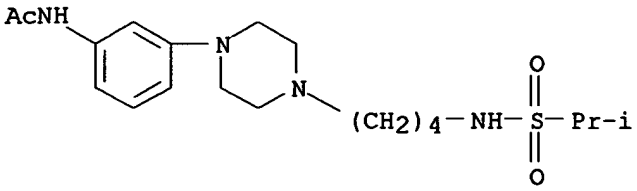
RN 740872-96-2 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(2-pyridinyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



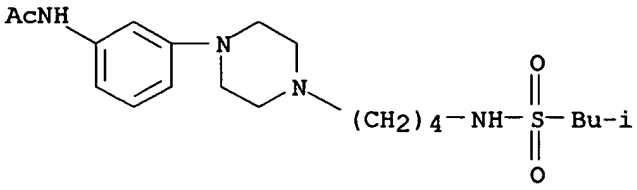
RN 740873-08-9 CAPLUS
CN Cyclopropanecarboxamide, N-[3-[4-[4-[[(cyclohexylmethyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



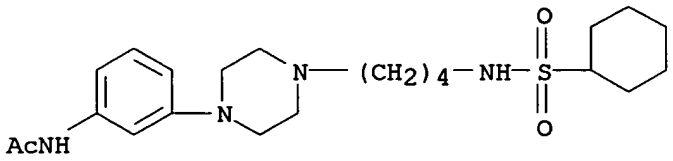
RN 740873-12-5 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(1-methylethyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



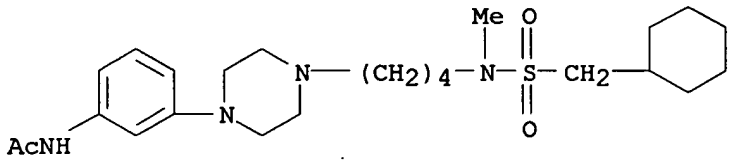
RN 740873-15-8 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(2-methylpropyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



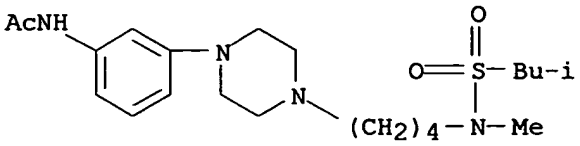
RN 740873-18-1 CAPLUS
CN Acetamide, N-[3-[4-[4-[(cyclohexylsulfonyl)amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



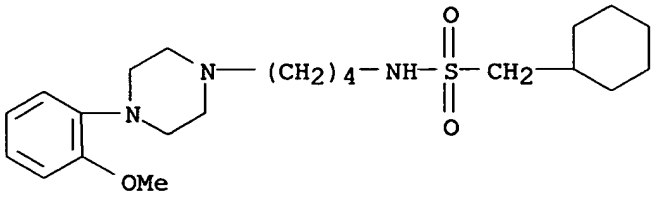
RN 740873-25-0 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(cyclohexylmethyl)sulfonyl]methylamino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



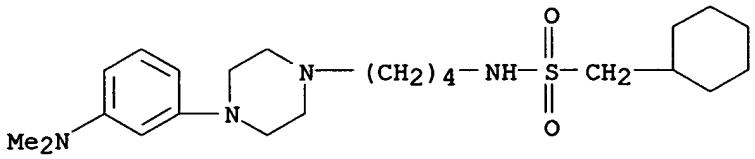
RN 740873-29-4 CAPLUS
CN Acetamide, N-[3-[4-[4-[methyl[(2-methylpropyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



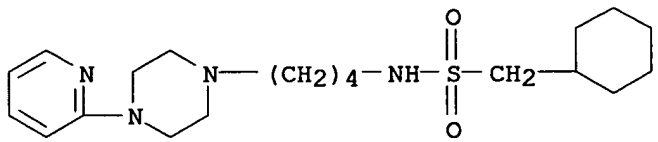
RN 740873-33-0 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-(2-methoxyphenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



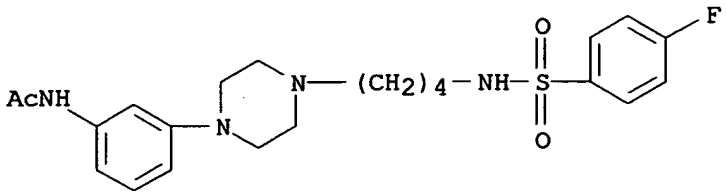
RN 740873-36-3 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-[3-(dimethylamino)phenyl]-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



RN 740873-40-9 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-(2-pyridinyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



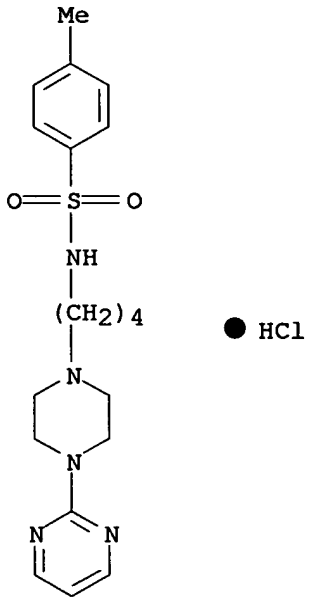
RN 740873-55-6 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(4-fluorophenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



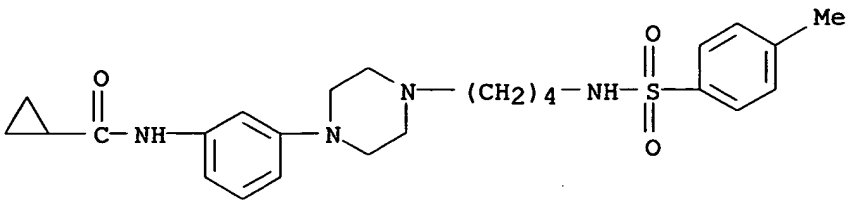
IT **91517-09-8P**, 4-Methyl-N-[4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl]benzenesulfonamide monohydrochloride **740872-84-8P**, Cyclopropanecarboxylic acid N-[3-[4-[4-[(4-tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]amide dihydrochloride **740872-85-9P**, N-[3-[4-[4-[(4-Tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]isobutyramide **740872-86-0P**, N-[3-[4-[4-[(4-Tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]butyramide **740872-87-1P**, 2,2-Dimethyl-N-[3-[4-[4-[(4-tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]propionamide **740872-89-3P**, N-[3-[4-[4-[(4-Tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide dihydrochloride **740872-90-6P**, N-[3-[4-[4-[(4-Tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]propionamide **740872-91-7P**, N-[4-[4-[3-[(Methanesulfonyl)amino]phenyl]piperazin-1-yl]butyl]-4-methylbenzenesulfonamide **740872-92-8P**, 4-Methyl-N-[4-[4-[3-[(propan-2-ylsulfonyl)amino]phenyl]piperazin-1-yl]butyl]benzenesulfonamide **740872-93-9P**, N-[4-[4-[3-[(Ethanesulfonyl)amino]phenyl]piperazin-1-yl]butyl]-4-methylbenzenesulfonamide **740872-94-0P**, 4-Methyl-N-[4-(4-phenylpiperazin-1-yl)butyl]-5-benzenesulfonamide **740872-95-1P**, 4-Methyl-N-[4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl]benzenesulfonamide dihydrochloride **740872-97-3P**, 4-Methyl-N-[4-[4-(pyridin-2-yl)piperazin-1-yl]butyl]benzenesulfonamide trihydrochloride **740872-98-4P**, N-[4-[4-(2-Methoxy-5-nitrophenyl)piperazin-1-yl]butyl]-4-methylbenzenesulfonamide **740873-07-8P 740873-09-0P 740873-13-6P**, N-[3-[4-[4-[(Propan-2-ylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide dihydrochloride **740873-16-9P**, N-[3-[4-[4-[(2-Methylpropan-1-ylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide dihydrochloride **740873-19-2P** **740873-26-1P**, N-[3-[4-[4-[(Cyclohexylmethylsulfonyl)(methyl)amino]butyl]piperazin-1-yl]phenyl]acetamide dihydrochloride **740873-30-7P** **740873-34-1P**, 1-Cyclohexyl-N-[4-[4-(2-methoxyphenyl)piperazin-1-yl]butyl]methanesulfonamide dihydrochloride **740873-37-4P**, 1-Cyclohexyl-N-[4-[4-(3-dimethylaminophenyl)piperazin-1-yl]butyl]methanesulfonamide trihydrochloride **740873-41-0P** **740873-56-7P 740873-66-9P**, 4-Methyl-N-[4-[4-(3-nitrophenyl)piperazin-1-yl]butyl]benzenesulfonamide monohydrochloride **740873-67-0P**, N-[4-[4-(3-Methoxyphenyl)piperazin-1-yl]butyl]-4-methylbenzenesulfonamide **740873-68-1P**, 4-Methyl-N-[4-[4-[3-(pyrazin-2-yl)phenyl]piperazin-1-yl]butyl]benzenesulfonamide **740873-69-2P**, N-[4-[4-(Biphenyl-3-yl)piperazin-1-yl]butyl]-4-methylbenzenesulfonamide **740873-70-5P**, 4-Methyl-N-[4-(4-phenylpiperazin-1-yl)butyl]benzenesulfonamide **740873-72-7P**, Cyclopropanecarboxylic acid N-[3-[4-[4-[(4-tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]amide monohydrochloride **740873-73-8P**, 4-Methyl-N-[4-[4-(pyridin-2-yl)piperazin-1-yl]butyl]benzenesulfonamide monohydrochloride **740873-74-9P**, 1-Cyclohexyl-N-[4-[4-(2-methoxyphenyl)piperazin-1-yl]butyl]methanesulfonamide monohydrochloride

**740873-75-0P**, N-[3-[4-[4-[(4-Tolylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide monohydrochloride **740873-78-3P**, 1-Cyclohexyl-N-[4-[4-(3-dimethylaminophenyl)piperazin-1-yl]butyl]methanesulfonamide monohydrochloride **740873-79-4P**, 1-Cyclohexyl-N-[4-[4-(pyridin-2-yl)piperazin-1-yl]butyl]methanesulfonamide monohydrochloride **740873-82-9P**, N-[3-[4-[4-[(Cyclohexylmethylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide monohydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(5-HT1 agonist; prepn. of arylpiperazinyl sulfonamides as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating anxiety and related disorders)

RN 91517-09-8 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-, monohydrochloride (9CI) (CA INDEX NAME)

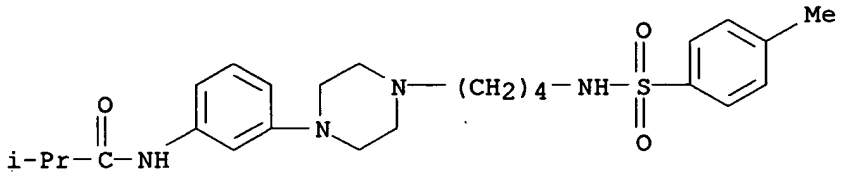



RN 740872-84-8 CAPLUS
CN Cyclopropanecarboxamide, N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)

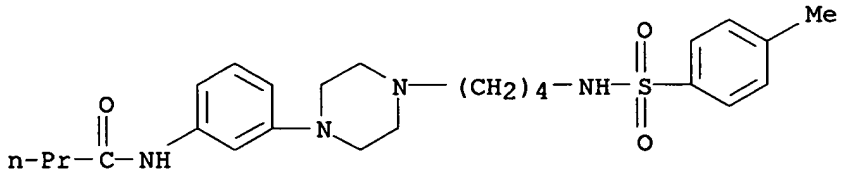


●2 HCl

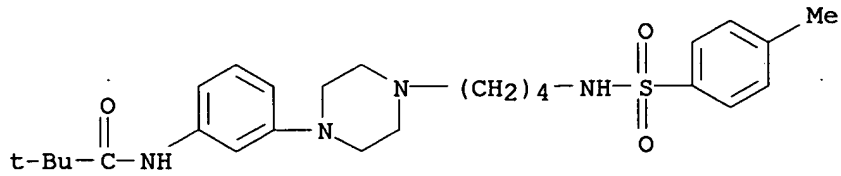
RN 740872-85-9 CAPLUS
CN Propanamide, 2-methyl-N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



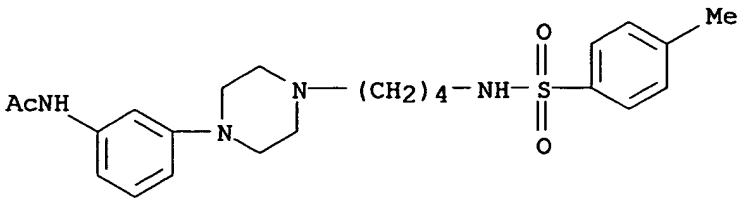
RN 740872-86-0 CAPLUS
CN Butanamide, N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



RN 740872-87-1 CAPLUS
CN Propanamide, 2,2-dimethyl-N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)

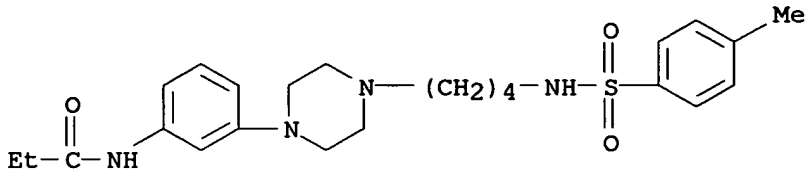


RN 740872-89-3 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)

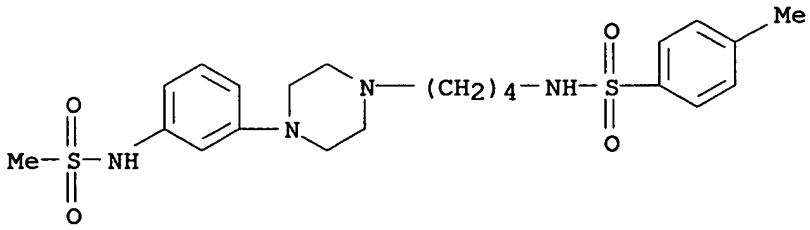


●2 HCl

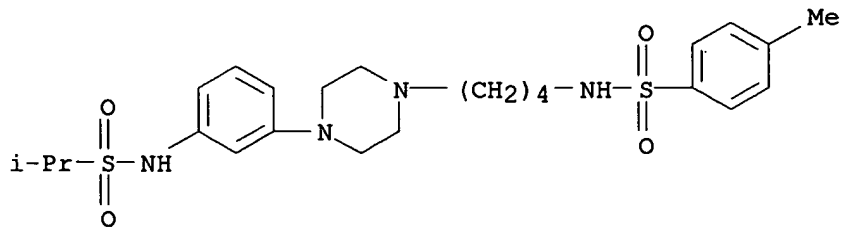
RN 740872-90-6 CAPLUS
CN Propanamide, N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



RN 740872-91-7 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-[3-[(methylsulfonyl)amino]phenyl]-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)

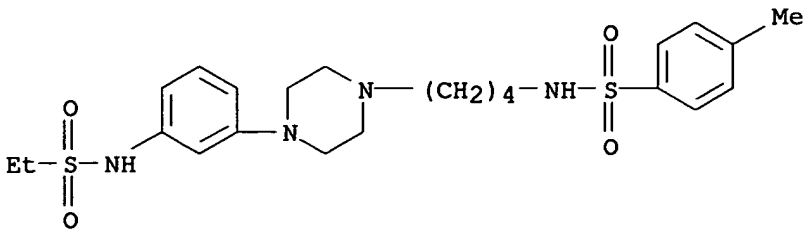


RN 740872-92-8 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-[3-[[(1-methylethyl)sulfonyl]amino]phenyl]-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)

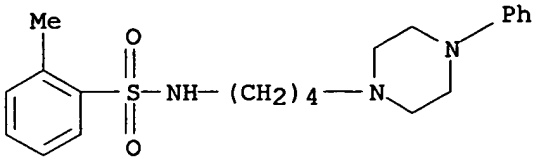


RN 740872-93-9 CAPLUS
CN Benzenesulfonamide, N-[4-[4-[3-[(ethylsulfonyl)amino]phenyl]-1-

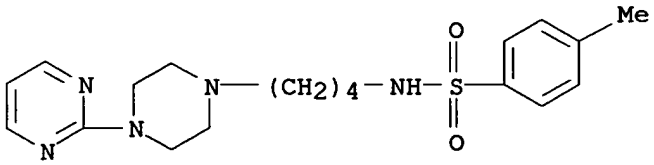
piperazinyl]butyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 740872-94-0 CAPLUS
CN Benzenesulfonamide, 2-methyl-N-[4-(4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)

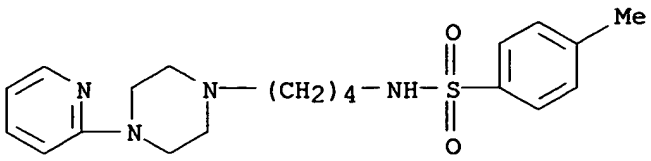


RN 740872-95-1 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-, dihydrochloride (9CI) (CA INDEX NAME)



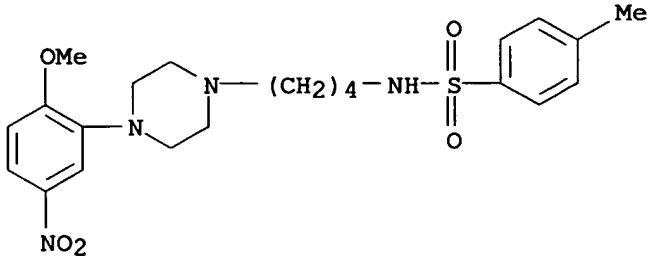
●2 HCl

RN 740872-97-3 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(2-pyridinyl)-1-piperazinyl]butyl]-, trihydrochloride (9CI) (CA INDEX NAME)

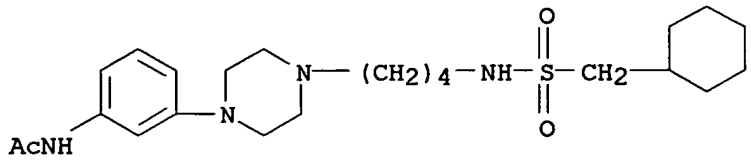


●3 HCl

RN 740872-98-4 CAPLUS
CN Benzenesulfonamide, N-[4-[4-(2-methoxy-5-nitrophenyl)-1-piperazinyl]butyl]-4-methyl- (9CI) (CA INDEX NAME)

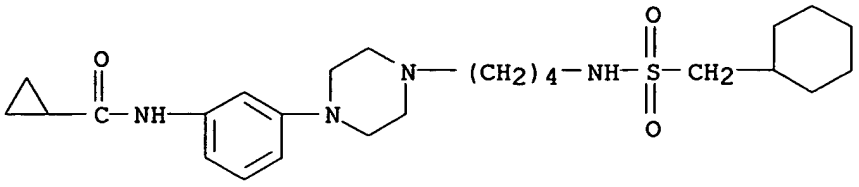


RN 740873-07-8 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(cyclohexylmethyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



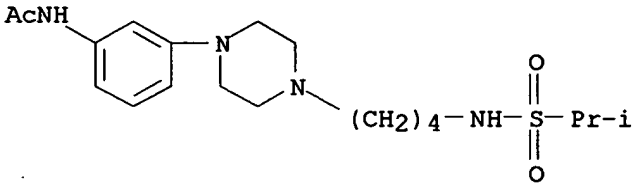
●2 HCl

RN 740873-09-0 CAPLUS
CN Cyclopropanecarboxamide, N-[3-[4-[4-[[(cyclohexylmethyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



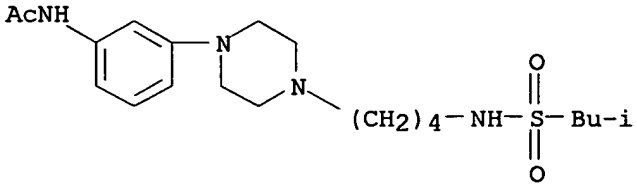
●2 HCl

RN 740873-13-6 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(1-methylethyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



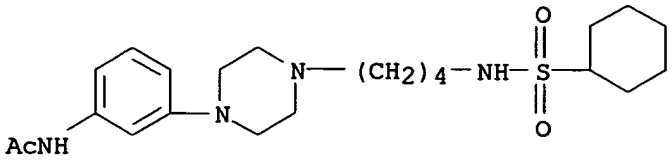
●2 HCl

RN 740873-16-9 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(2-methylpropyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



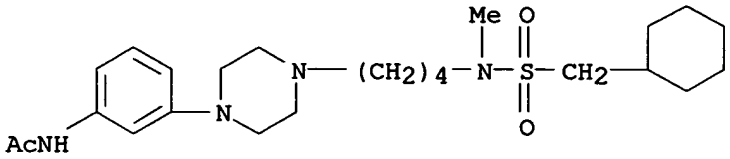
●2 HCl

RN 740873-19-2 CAPLUS
CN Acetamide, N-[3-[4-[4-[(cyclohexylsulfonyl)amino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



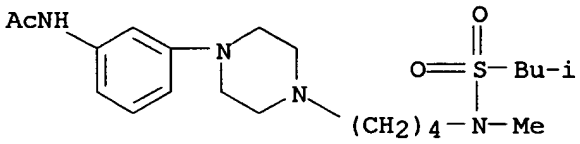
●2 HCl

RN 740873-26-1 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(cyclohexylmethyl)sulfonyl]methylamino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



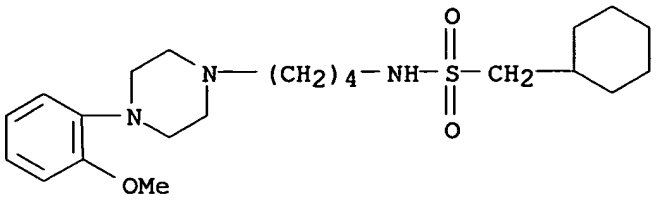
●2 HCl

RN 740873-30-7 CAPLUS
CN Acetamide, N-[3-[4-[4-[methyl[(2-methylpropyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



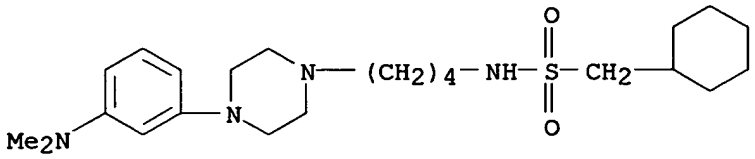
●2 HCl

RN 740873-34-1 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-(2-methoxyphenyl)-1-piperazinyl]butyl]-, dihydrochloride (9CI) (CA INDEX NAME)



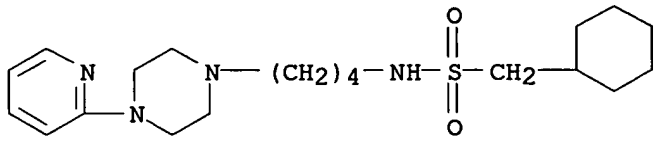
●2 HCl

RN 740873-37-4 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-[3-(dimethylamino)phenyl]-1-piperazinyl]butyl]-, trihydrochloride (9CI) (CA INDEX NAME)



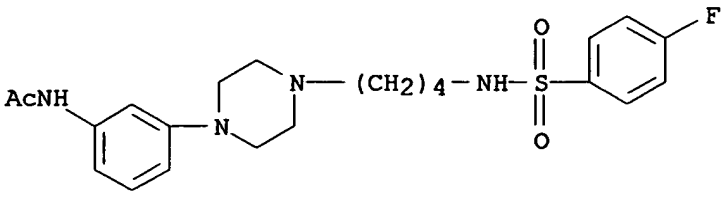
●3 HCl

RN 740873-41-0 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-(2-pyridinyl)-1-piperazinyl]butyl]-, trihydrochloride (9CI) (CA INDEX NAME)



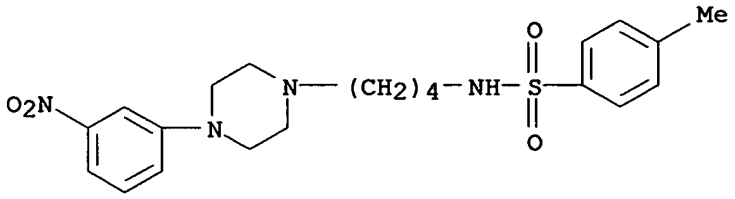
●3 HCl

RN 740873-56-7 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(4-fluorophenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



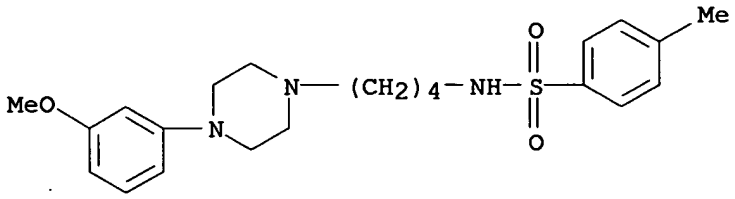
●2 HCl

RN 740873-66-9 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(3-nitrophenyl)-1-piperazinyl]butyl]-, monohydrochloride (9CI) (CA INDEX NAME)

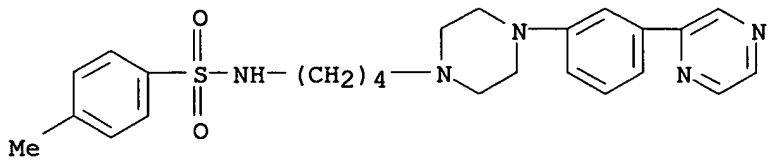


● HCl

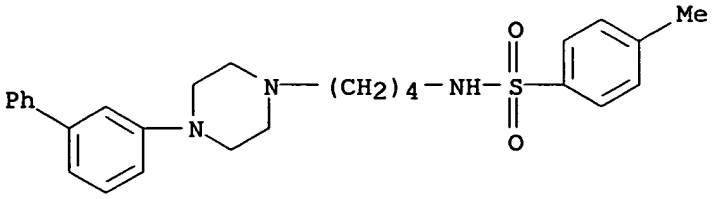
RN 740873-67-0 CAPLUS
CN Benzenesulfonamide, N-[4-[4-(3-methoxyphenyl)-1-piperazinyl]butyl]-4-methyl- (9CI) (CA INDEX NAME)



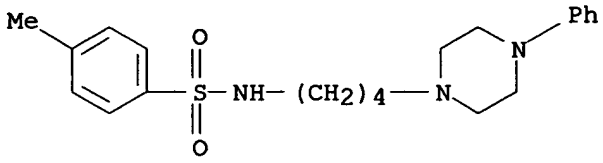
RN 740873-68-1 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(3-pyrazinylphenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



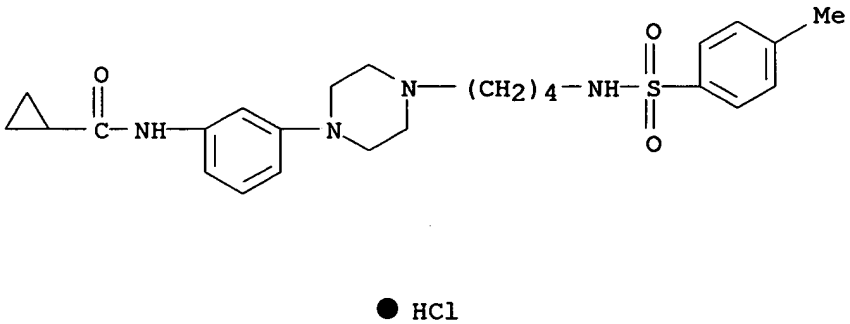
RN 740873-69-2 CAPLUS
CN Benzenesulfonamide, N-[4-(4-[1,1'-biphenyl]-3-yl-1-piperazinyl)butyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 740873-70-5 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-(4-phenyl-1-piperazinyl)butyl]- (9CI) (CA INDEX NAME)

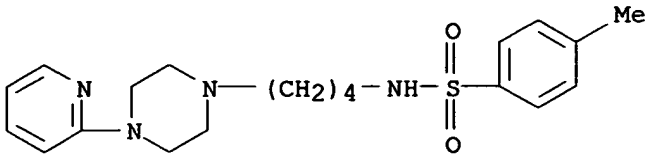


RN 740873-72-7 CAPLUS
CN Cyclopropanecarboxamide, N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



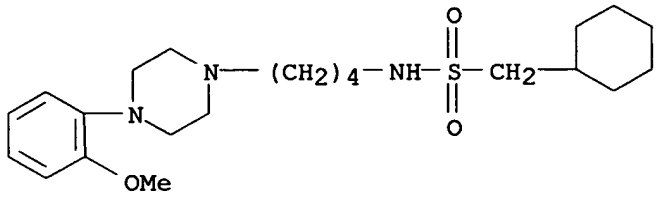
● HCl

RN 740873-73-8 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(2-pyridinyl)-1-piperazinyl]butyl]-, monohydrochloride (9CI) (CA INDEX NAME)



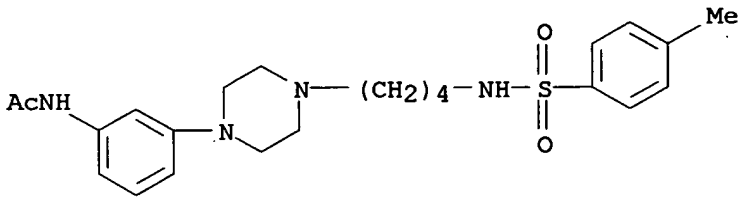
● HCl

RN 740873-74-9 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-(2-methoxyphenyl)-1-piperazinyl]butyl]-, monohydrochloride (9CI) (CA INDEX NAME)



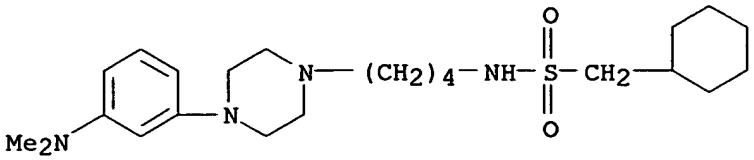
● HCl

RN 740873-75-0 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(4-methylphenyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



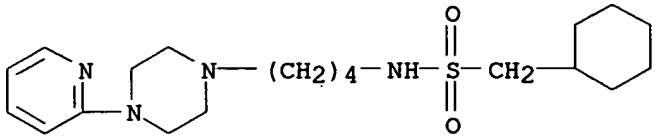
● HCl

RN 740873-78-3 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-[3-(dimethylamino)phenyl]-1-piperazinyl]butyl]-, monohydrochloride (9CI) (CA INDEX NAME)



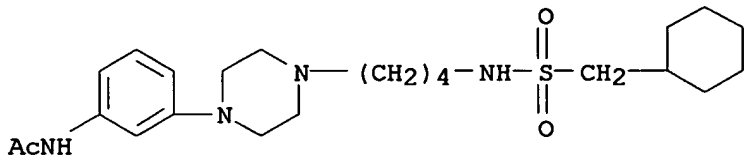
● HCl

RN 740873-79-4 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-(2-pyridinyl)-1-piperazinyl]butyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

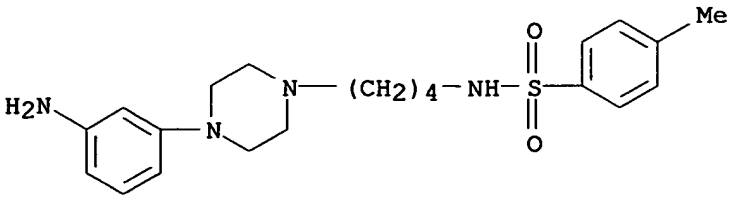
RN 740873-82-9 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(cyclohexylmethyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



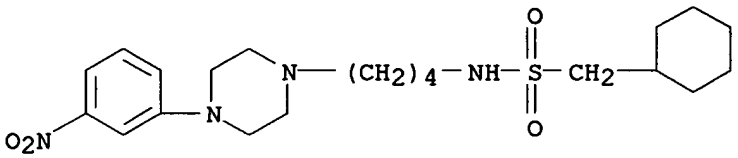
● HCl

IT **740872-82-6P**, 3-[4-[4-(Tosylamino)butyl]piperazin-1-yl]benzeneamine **740873-04-5P 740873-05-6P**
**740873-06-7P**, N-[3-[4-[4-[(Cyclohexylmethylsulfonyl)amino]butyl]piperazin-1-yl]phenyl]acetamide **740873-10-3P 740873-11-4P**
**740873-14-7P 740873-23-8P 740873-24-9P**
**740873-27-2P 740873-28-3P 740873-53-4P**
**740873-54-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of arylpiperazinyl sulfonamides as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating anxiety and related disorders)

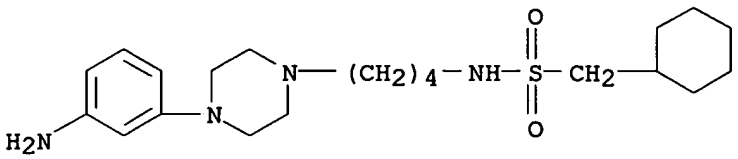
RN 740872-82-6 CAPLUS
CN Benzenesulfonamide, N-[4-[4-(3-aminophenyl)-1-piperazinyl]butyl]-4-methyl- (9CI) (CA INDEX NAME)



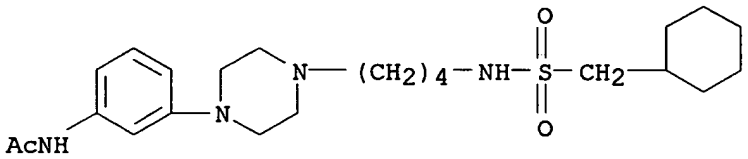
RN 740873-04-5 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-(3-nitrophenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



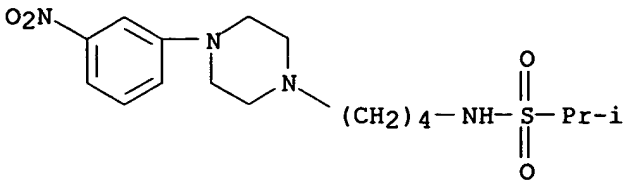
RN 740873-05-6 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-(3-aminophenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



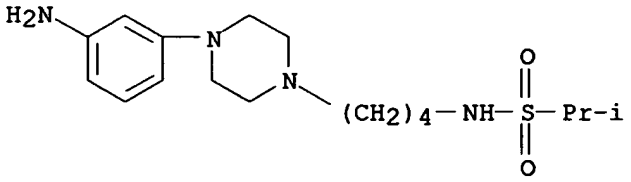
RN 740873-06-7 CAPLUS
CN Acetamide, N-[3-[4-[4-[[(cyclohexylmethyl)sulfonyl]amino]butyl]-1-piperazinyl]phenyl]- (9CI) (CA INDEX NAME)



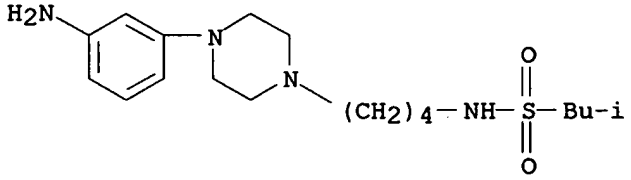
RN 740873-10-3 CAPLUS
CN 2-Propanesulfonamide, N-[4-[4-(3-nitrophenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



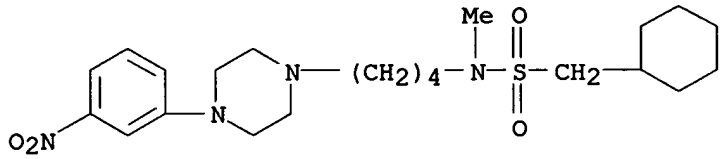
RN 740873-11-4 CAPLUS
CN 2-Propanesulfonamide, N-[4-[4-(3-aminophenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



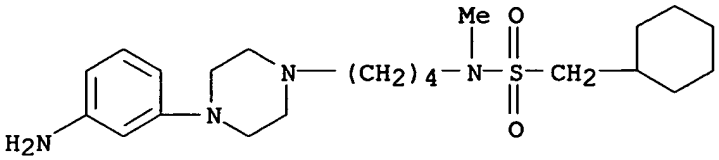
RN 740873-14-7 CAPLUS
CN 1-Propanesulfonamide, N-[4-[4-(3-aminophenyl)-1-piperazinyl]butyl]-2-methyl- (9CI) (CA INDEX NAME)



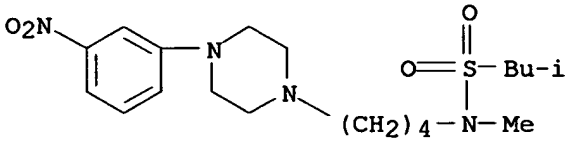
RN 740873-23-8 CAPLUS
CN Cyclohexanemethanesulfonamide, N-methyl-N-[4-[4-(3-nitrophenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



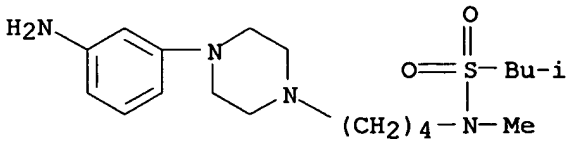
RN 740873-24-9 CAPLUS
CN Cyclohexanemethanesulfonamide, N-[4-[4-(3-aminophenyl)-1-piperazinyl]butyl]-N-methyl- (9CI) (CA INDEX NAME)



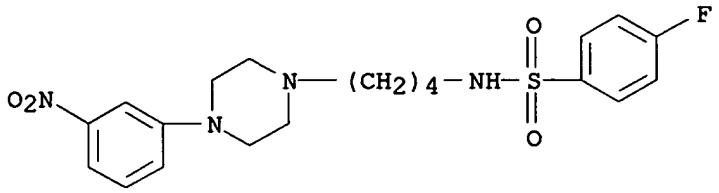
RN 740873-27-2 CAPLUS
CN 1-Propanesulfonamide, N,2-dimethyl-N-[4-[4-(3-nitrophenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



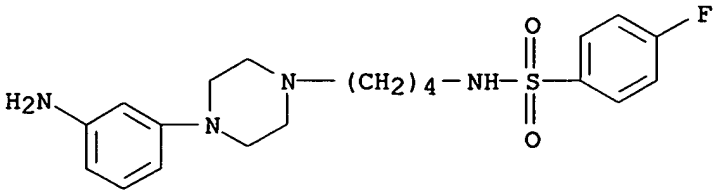
RN 740873-28-3 CAPLUS
CN 1-Propanesulfonamide, N-[4-[4-(3-aminophenyl)-1-piperazinyl]butyl]-N,2-dimethyl- (9CI) (CA INDEX NAME)



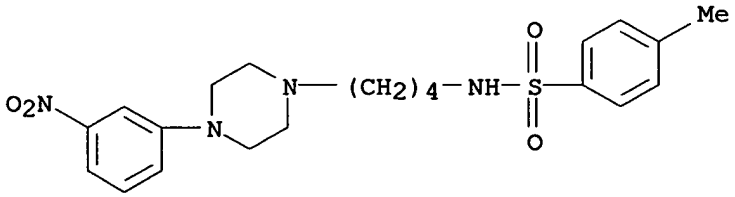
RN 740873-53-4 CAPLUS
CN Benzenesulfonamide, 4-fluoro-N-[4-[4-(3-nitrophenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)



RN 740873-54-5 CAPLUS
CN Benzenesulfonamide, N-[4-[4-(3-aminophenyl)-1-piperazinyl]butyl]-4-fluoro- (9CI) (CA INDEX NAME)

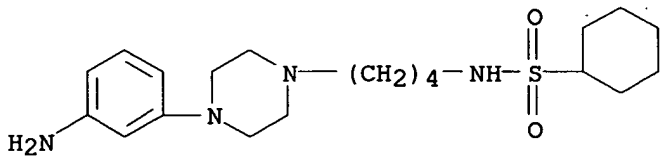


IT **740872-81-5P**, 4-Methyl-N-[4-[4-(3-nitrophenyl)piperazin-1-yl]butyl]benzenesulfonamide dihydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylpiperazinyl sulfonamides as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating anxiety and related disorders)
RN 740872-81-5 CAPLUS
CN Benzenesulfonamide, 4-methyl-N-[4-[4-(3-nitrophenyl)-1-piperazinyl]butyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

IT **740873-17-0**, Cyclohexanesulfonic acid [4-[4-(3-aminophenyl)piperazin-1-yl]butyl]amide
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of arylpiperazinyl sulfonamides as 5-HT, in particular 5-HT1, receptor agonists and antagonists for treating anxiety and related disorders)
RN 740873-17-0 CAPLUS
CN Cyclohexanesulfonamide, N-[4-[4-(3-aminophenyl)-1-piperazinyl]butyl]- (9CI) (CA INDEX NAME)

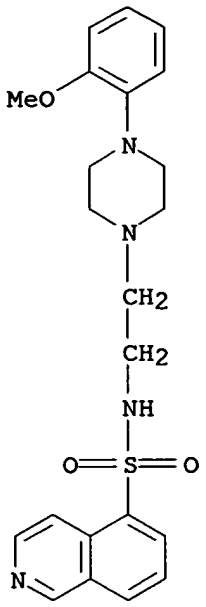


L3 ANSWER 19 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:444494 CAPLUS

DN 137:28321
TI Use of certain isoquinolinesulfonyl compounds for the treatment of glaucoma and ocular ischemia
IN Hellberg, Mark R.; Kapin, Michael A.; Desantis, Louis M., Jr.
PA Alcon Laboratories, Inc., USA
SO U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 77,575.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 6403590 | B1 | 20020611 | US 2001-919301 | 20010731 |
| | WO 9723222 | A1 | 19970703 | WO 1996-US20197 | 19961220 |
| | W: AU, CA, CN, JP, KR, MX, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | US 6271224 | B1 | 20010807 | US 1999-77575 | 19990119 |
| PRAI | US 1995-9351P | P | 19951221 | | |
| | WO 1996-US20197 | W | 19961220 | | |
| | US 1999-77575 | A2 | 19990119 | | |

OS MARPAT 137:28321
AB Isoquinolinesulfonyl compds. are used in ophthalmic compns. to treat glaucoma or other ischemic-borne ocular disorders, e.g. retinopathies or optic neuropathies. These compds. vasodilate ocular blood vessels, lower IOP and prevent or reduce the progression of visual field loss. Prepn. and testing of 1-(5-isoquinolinesulfonyl)-2,5-dimethylpiperazine are described.
IT **192712-45-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isoquinolinesulfonyl compds. for treatment of glaucoma and ocular ischemia)
RN 192712-45-1 CAPLUS
CN 5-Isoquinolinesulfonamide, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-(9CI) (CA INDEX NAME)



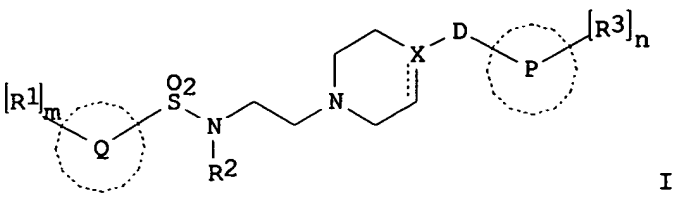
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 29 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:688218 CAPLUS
DN 133:252456
TI Preparation of N-[2-piperazino(or piperidino)ethyl] benzenesulfonamides and thiophenesulfonamides as 5-HT7 receptor antagonists
IN Lovell, Peter John
PA Smithkline Beecham Plc, UK
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

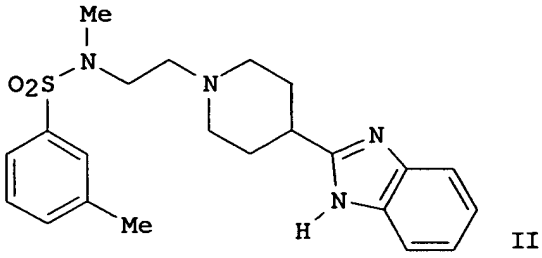
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000056712 | A1 | 20000928 | WO 2000-EP2267 | 20000314 |
| | W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1163221 | A1 | 20011219 | EP 2000-916945 | 20000314 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | US 6660751 | B1 | 20031209 | US 2001-937043 | 20010920 |
| PRAI | GB 1999-6624 | A | 19990323 | | |
| | WO 2000-EP2267 | W | 20000314 | | |

OS MARPAT 133:252456

GI



I



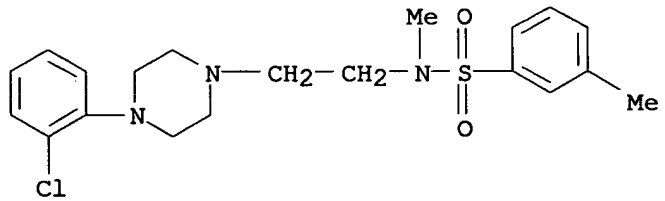
II

AB The title compds. [I; Q = Ph, thienyl; R1 = halo, OH, alkyl, etc.; m = 0-3; R2 = alkyl; X = N, C, CH; D = a single bond; CO, O, CH2 subject to the proviso that when X = N then D is not O; P = Ph, naphthyl, 5-6 membered heteroaryl contg. 1-3 heteroatoms selected from O, N and S, etc.; R3 = (un)substituted alkyl; n = 0-3] having 5-HT7 receptor antagonist activity, and therefore useful in the treatment of CNS and other disorders, were prepd. E.g., a multi-step synthesis of benzenesulfonamide II was given. All compds. I tested had a pKi of 6.2-9.0 against 5-HT7 receptor binding.

IT **295790-23-7P 295790-24-8P 295790-25-9P**
**295790-26-0P 295790-32-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-[2-piperazino(or piperidino)ethyl] benzenesulfonamides and thiophenesulfonamides as 5-HT7 receptor antagonists)

RN 295790-23-7 CAPLUS

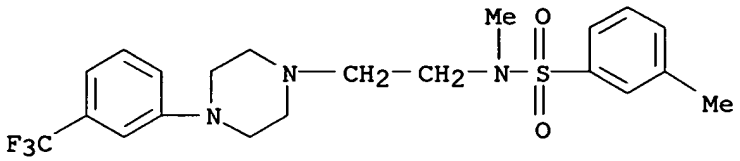
CN Benzenesulfonamide, N-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)



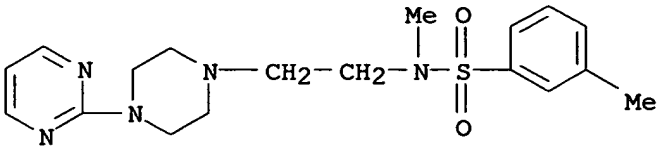
RN 295790-24-8 CAPLUS

CN Benzenesulfonamide, N,3-dimethyl-N-[2-[4-[3-(trifluoromethyl)phenyl]-1-

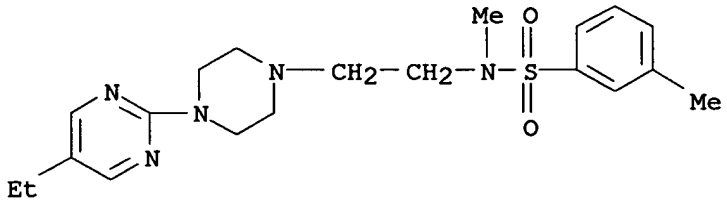
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



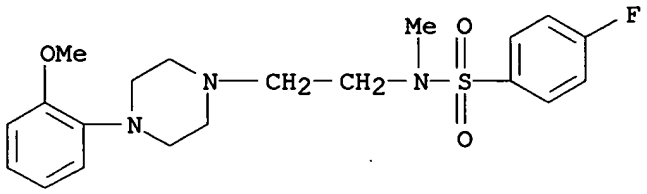
RN 295790-25-9 CAPLUS
CN Benzenesulfonamide, N,3-dimethyl-N-[2-[4-(2-pyrimidinyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 295790-26-0 CAPLUS
CN Benzenesulfonamide, N-[2-[4-(5-ethyl-2-pyrimidinyl)-1-piperazinyl]ethyl]-N,3-dimethyl- (9CI) (CA INDEX NAME)

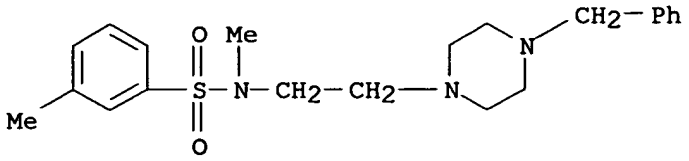


RN 295790-32-8 CAPLUS
CN Benzenesulfonamide, 4-fluoro-N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-methyl- (9CI) (CA INDEX NAME)



IT **295790-51-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-[2-piperazino(or piperidino)ethyl] benzenesulfonamides and thiophenesulfonamides as 5-HT7 receptor antagonists)
RN 295790-51-1 CAPLUS
CN Benzenesulfonamide, N,3-dimethyl-N-[2-[4-(phenylmethyl)-1-

piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

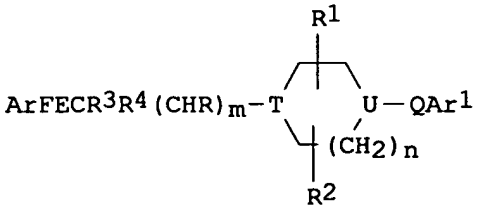


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 34 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:147946 CAPLUS
DN 130:196670
TI Arylcarbamoylalkylpiperazines and -piperidines as CCR-3-receptor antagonists
IN Gong, Leyi; Kertesz, Denis John; Smith, David Bernard; Talamas, Francisco Xavier; Wilhelm, Robert Stephen
PA F. Hoffmann-La Roche A.-G., Switz.
SO Ger. Offen., 60 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE 19837386 | A1 | 19990225 | DE 1998-19837386 | 19980818 |
| | EP 903349 | A2 | 19990324 | EP 1998-114971 | 19980810 |
| | EP 903349 | A3 | 20000524 | | |
| | EP 903349 | B1 | 20060104 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY | | | | |
| | NZ 331319 | A | 20000327 | NZ 1998-331319 | 19980811 |
| | CA 2245043 | AA | 19990218 | CA 1998-2245043 | 19980814 |
| | ES 2154167 | A1 | 20010316 | ES 1998-1760 | 19980814 |
| | ES 2154167 | B1 | 20011101 | | |
| | NO 9803749 | A | 19990219 | NO 1998-3749 | 19980817 |
| | GB 2330580 | A1 | 19990428 | GB 1998-17910 | 19980817 |
| | AU 9880800 | A1 | 19990225 | AU 1998-80800 | 19980818 |
| | AU 744059 | B2 | 20020214 | | |
| | FR 2767826 | A1 | 19990305 | FR 1998-10504 | 19980818 |
| | CN 1211572 | A | 19990324 | CN 1998-117990 | 19980818 |
| | CN 1107061 | B | 20030430 | | |
| | JP 11147872 | A2 | 19990602 | JP 1998-231918 | 19980818 |
| | JP 3014367 | B2 | 20000228 | | |
| | SG 70110 | A1 | 20000125 | SG 1998-3133 | 19980818 |
| | BR 9803179 | A | 20000328 | BR 1998-3179 | 19980818 |
| | IT 1304150 | B1 | 20010308 | IT 1998-MI1902 | 19980818 |
| | US 2004266782 | A1 | 20041230 | US 2003-719204 | 20031121 |
| | US 6984637 | B2 | 20060110 | | |
| PRAI | US 1997-56001P | P | 19970818 | | |
| | US 1998-134013 | A3 | 19980814 | | |
| | US 2001-965068 | A3 | 20010926 | | |

OS MARPAT 130:196670
GI



I

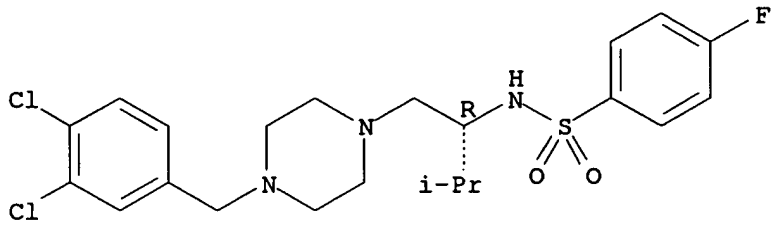
AB Title compds. I [Ar, Ar1 = aryl, heteroaryl; E = (un)substituted CONH, SO2NH, NHCONH, NHSO2NH, NHCSNH, NHCO, NHCO2, O2CNH, NHSO2; F = alkylene, alkenylene; R = H, alkyl; R1, R2 = H, alkyl; R3, R4 = H, (un)substituted alkyl, cycloalkyl, heterocyclic, CN; CR3R4 = carbocyclic, heterocyclic; RR3 = atoms required to form a carbocyclic or heterocyclic ring; Q = (un)substituted alkylene, heteroalkylene; one of T an U = N, the other is N or CH; n = 0-2] were prepd. for use as CCR-3 receptor antagonists, useful in treating asthma in particular. Thus, N-[(1S)-[4-(3,4-dichlorobenzyl)piperazin-1-ylmethyl]-2-methylpropyl]-4-methylbenzamide.2HCl was prepd. from 1-(3,4-dichlorobenzyl)piperazine and BOC-L-valine in 4 steps. This compd. had an IC50 for CCR-3 receptor binding of 0.24 .mu.M.

IT **220772-02-1P 220772-03-2P 220772-06-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylcarbamoylalkylpiperazines and -piperidines as CCR-3-receptor antagonists)

RN 220772-02-1 CAPLUS

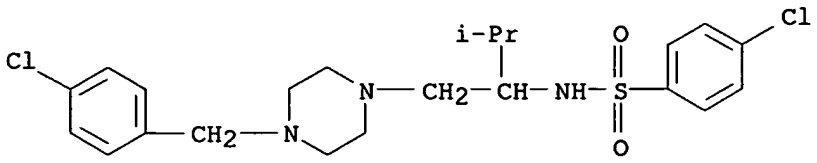
CN Benzenesulfonamide, N-[(1R)-1-[[4-[(3,4-dichlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]-4-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

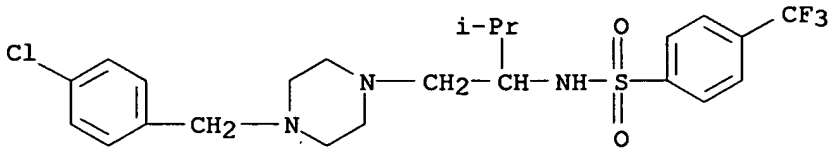


RN 220772-03-2 CAPLUS

CN Benzenesulfonamide, 4-chloro-N-[1-[[4-[(4-chlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

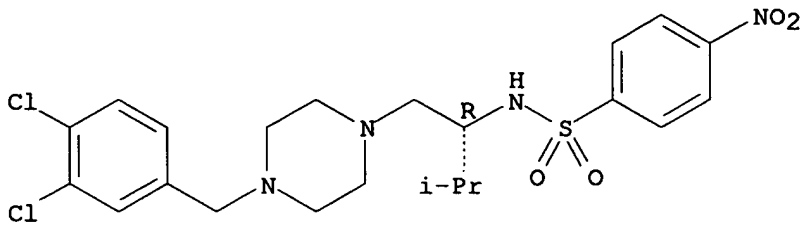


RN 220772-06-5 CAPLUS
CN Benzenesulfonamide, N-[1-[[4-[(4-chlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



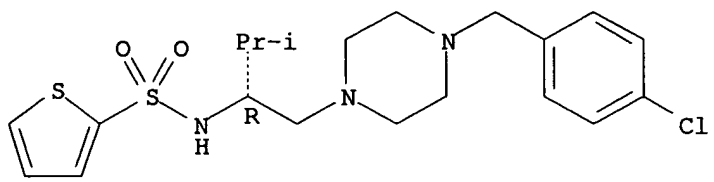
IT **220772-04-3P 220772-05-4P 220772-07-6P**
**220772-08-7P 220772-09-8P 220772-10-1P**
**220772-11-2P 220772-12-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylcarbamoylalkylpiperazines and -piperidines as CCR-3-receptor antagonists)
RN 220772-04-3 CAPLUS
CN Benzenesulfonamide, N-[(1R)-1-[[4-[(3,4-dichlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]-4-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

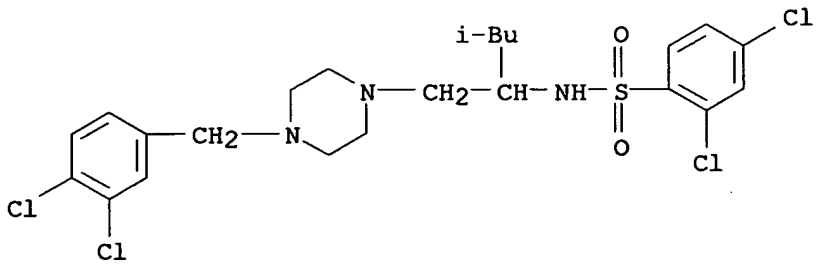


RN 220772-05-4 CAPLUS
CN 2-Thiophenesulfonamide, N-[(1R)-1-[[4-[(4-chlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

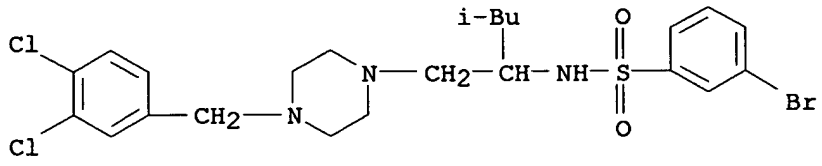
Absolute stereochemistry.



RN 220772-07-6 CAPLUS
CN Benzenesulfonamide, 2,4-dichloro-N-[1-[[4-[(3,4-dichlorophenyl)methyl]-1-piperazinyl]methyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)

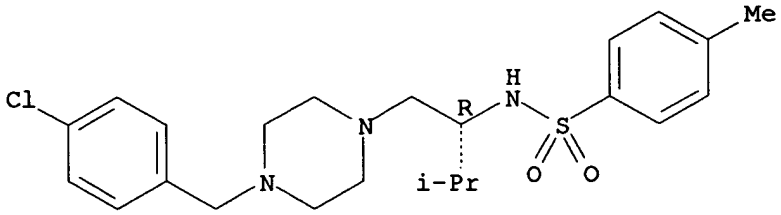


RN 220772-08-7 CAPLUS
CN Benzenesulfonamide, 3-bromo-N-[1-[[4-[(3,4-dichlorophenyl)methyl]-1-piperazinyl]methyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)



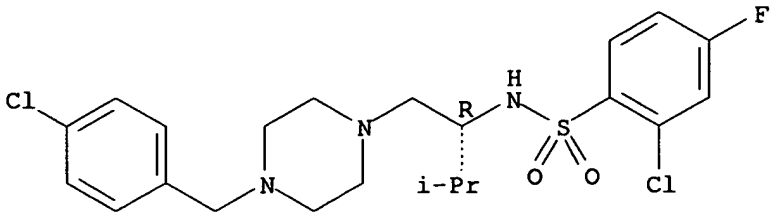
RN 220772-09-8 CAPLUS
CN Benzenesulfonamide, N-[(1R)-1-[[4-[(4-chlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



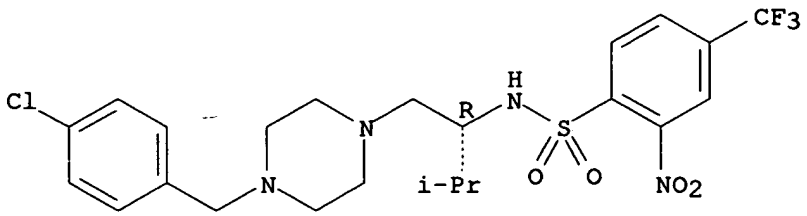
RN 220772-10-1 CAPLUS
CN Benzenesulfonamide, 2-chloro-N-[(1R)-1-[[4-[(4-chlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]-4-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

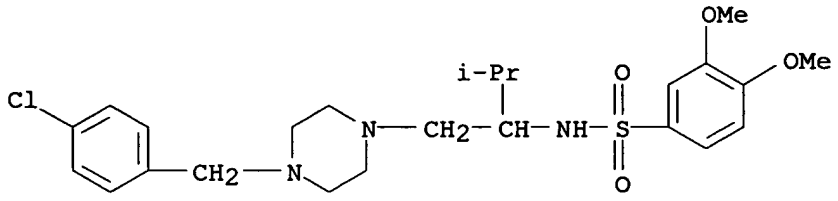


RN 220772-11-2 CAPLUS
CN Benzenesulfonamide, N-[(1R)-1-[[4-[(4-chlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]-2-nitro-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220772-12-3 CAPLUS
CN Benzenesulfonamide, N-[1-[[4-[(4-chlorophenyl)methyl]-1-piperazinyl]methyl]-2-methylpropyl]-3,4-dimethoxy- (9CI) (CA INDEX NAME)

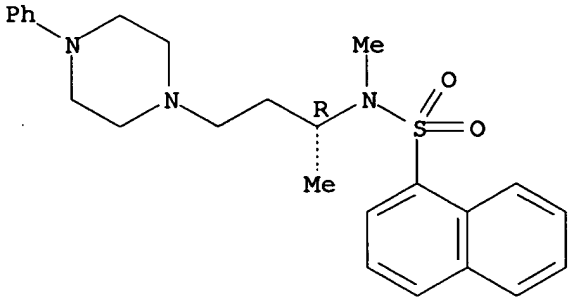


L3 ANSWER 40 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:542438 CAPLUS
DN 127:248014
TI Preparation of piperidinylpropylarenesulfonamide derivatives as 5HT7 receptor antagonists.
IN Forbes, Ian Thomson
PA Smithkline Beecham PLC, UK; Forbes, Ian Thomson
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9729097 | A1 | 19970814 | WO 1997-EP446 | 19970127 |

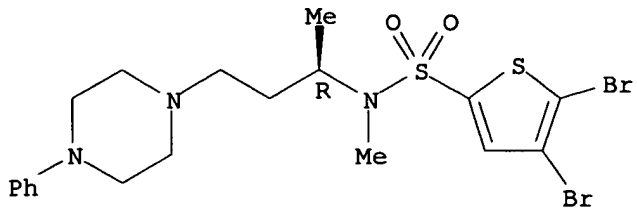
W: JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 883613 A1 19981216 EP 1997-902289 19970127
R: BE, CH, DE, ES, FR, GB, IT, LI, NL
JP 2000504677 T2 20000418 JP 1997-528118 19970127
PRAI GB 1996-2679 A 19960209
GB 1996-13263 A 19960625
WO 1997-EP446 W 19970127
OS MARPAT 127:248014
AB ArSO2NR1(CR2R3)nNR4R5 [Ar = (substituted) mono- or bicyclic (hetero)aryl; R1 = alkyl; R2, R3 = H, alkyl; R4, R5 = H, alkyl, aryl, aralkyl; NR4R5 = (substituted) 5-8 membered heterocyclyl; n = 2-4], were prepd. Thus, 1-methyl-3-(3-methylpiperidin-3-yl)propylamine and Et3N were treated with 1-naphthalenesulfonyl chloride in CH2Cl2 to give 48% N-[1-methyl-3-(3-methylpiperidin-1-yl)propyl]-1-naphthalenesulfonamide. The latter in DMF was treated with NaH and MeI in DMF to give 68% N-methyl-N-[1-methyl-3-(3-methylpiperidin-1-yl)propyl]-1-naphthalenesulfonamide, isolated as the hydrochloride. Title compds. showed pKi = <5.2-7.8 for displacing [3H]-carboxamidotryptamine from 5HT7 receptor clones.
IT **195199-77-0P 195199-78-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidinylpropylarenesulfonamide derivs. as 5HT7 receptor antagonists)
RN 195199-77-0 CAPLUS
CN 1-Naphthalenesulfonamide, N-methyl-N-[1-methyl-3-(4-phenyl-1-piperazinyl)propyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RN 195199-78-1 CAPLUS
CN 2-Thiophenesulfonamide, 4,5-dibromo-N-methyl-N-[1-methyl-3-(4-phenyl-1-piperazinyl)propyl]-, (R)- (9CI) (CA INDEX NAME)

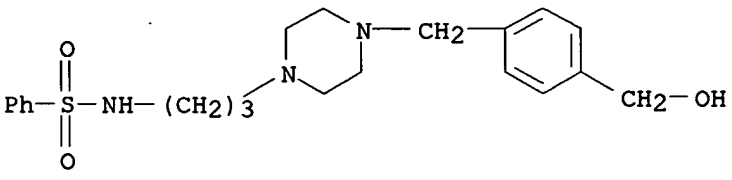
Absolute stereochemistry.



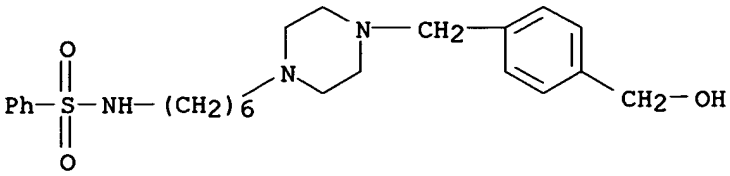
L3 ANSWER 41 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:526102 CAPLUS
DN 127:220471
TI Preparation of nitro compounds for treatment of angina pectoris and for prevention of restenosis after percutaneous transluminal coronary angioplasty
IN Uchida, Yasuyoshi; Koga, Hiroshi; Ko, Naoki
PA Chugai Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 30 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI JP 09202764 | A2 | 19970805 | JP 1996-43976 | 19960124 |
| PRAI JP 1996-43976 | | 19960124 | | |

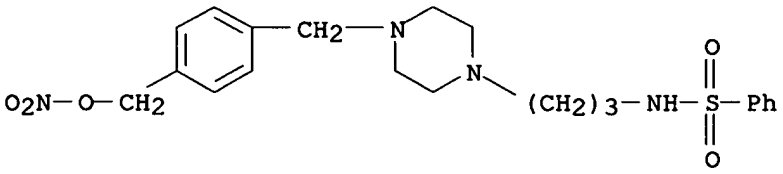
OS MARPAT 127:220471
AB R1AR2GR3ONO2 [R1 = (un)substituted Ph, naphthyl, anthryl, other arom. hydrocarbyl, (un)substituted pyridyl, quinolyl, isoquinolyl, carbazolyl, indolyl, other heterocyclyl; A = SO2, O, S, (N-substituted) sulfonamido, amido, thioamido, cyanamido; R2 = C1-10 hydrocarbyl; G = SO2, O, S, (N-substituted) sulfonamido, amido, thioamido, cyanamido, amino, cyclic amino; R3 = (un)substituted C1-18 hydrocarbyl (linked via hetero atom)] or their pharmaceutically acceptable salts are prepd. Mesylation of 3.0 g 5-chloro-N-(6-hydroxyhexyl)-1-naphthalenesulfonamide in CH2Cl2 in the presence of 4-dimethylaminopyridine at room temp. for 2.5 h gave 3.54 g 5-chloro-N-(6-methanesulfonyloxyhexyl)-1-naphthalenesulfonamide, which (1.77 g) was treated with 1.01 mL 2-aminoethanol in THF at 70.degree. for 27 h to afford 920 mg 5-chloro-N-[6-(2-hydroxyethylamino)hexyl]-1-naphthalenesulfonamide. The product (200 mg) was treated with urea, fuming HNO3, and Ac2O in CH2Cl2 at room temp. for 4 h to give 60 mg 5-chloro-N-[6-(2-nitroxyethylamino)hexyl]-1-naphthalenesulfonamide nitrate, which at 10-5 M inhibited 52% proliferation of rat vascular smooth muscle cells (A7r5 cells).
IT **195003-63-5P**, N-[3-[4-[4-(Hydroxymethyl)benzyl]piperazin-1-yl]propyl]benzenesulfonamide **195003-65-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of antianginal nitro compds.)
RN 195003-63-5 CAPLUS
CN Benzenesulfonamide, N-[3-[4-[[4-(hydroxymethyl)phenyl]methyl]-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



RN 195003-65-7 CAPLUS
CN Benzenesulfonamide, N-[6-[4-[[4-(hydroxymethyl)phenyl]methyl]-1-piperazinyl]hexyl]- (9CI) (CA INDEX NAME)

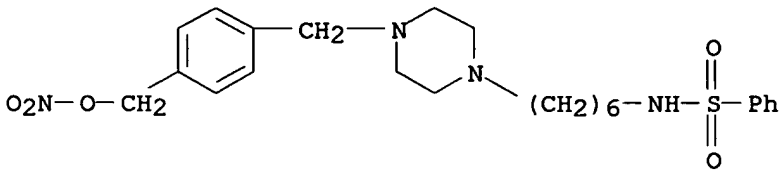


IT **195002-98-3P 195003-02-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antianginal nitro compds.)
RN 195002-98-3 CAPLUS
CN Benzenesulfonamide, N-[3-[4-[[4-[(nitrooxy)methyl]phenyl]methyl]-1-piperazinyl]propyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 195003-02-2 CAPLUS
CN Benzenesulfonamide, N-[6-[4-[[4-[(nitrooxy)methyl]phenyl]methyl]-1-piperazinyl]hexyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L3 ANSWER 42 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:503173 CAPLUS
DN 127:126664
TI Pharmaceutical compositions containing isoquinolinesulfonyl derivatives for the treatment of glaucoma and ocular ischemia
IN Kapin, Michael A.; Desantis, Louis M., Jr.
PA Alcon Laboratories, Inc., USA; Kapin, Michael A.; Desantis, Louis M., Jr.
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 2

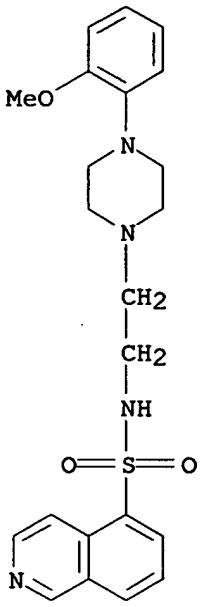
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9723222 | A1 | 19970703 | WO 1996-US20197 | 19961220 |
| | W: AU, CA, CN, JP, KR, MX, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | CA 2240271 | AA | 19970703 | CA 1996-2240271 | 19961220 |
| | CA 2240271 | C | 20051213 | | |
| | AU 9714644 | A1 | 19970717 | AU 1997-14644 | 19961220 |
| | AU 720326 | B2 | 20000525 | | |
| | EP 868186 | A1 | 19981007 | EP 1996-945220 | 19961220 |
| | EP 868186 | B1 | 20050302 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | CN 1207680 | A | 19990210 | CN 1996-199673 | 19961220 |
| | JP 2001509780 | T2 | 20010724 | JP 1997-523793 | 19961220 |
| | JP 3719609 | B2 | 20051124 | | |
| | AT 289815 | E | 20050315 | AT 1996-945220 | 19961220 |
| | PT 868186 | T | 20050531 | PT 1996-945220 | 19961220 |
| | ES 2238702 | T3 | 20050901 | ES 1996-945220 | 19961220 |
| | TW 534814 | B | 20030601 | TW 1997-86101346 | 19970204 |
| | US 6271224 | B1 | 20010807 | US 1999-77575 | 19990119 |
| | HK 1015691 | A1 | 20050520 | HK 1999-100710 | 19990227 |
| | US 6403590 | B1 | 20020611 | US 2001-919301 | 20010731 |
| PRAI | US 1995-9351P | P | 19951221 | | |
| | WO 1996-US20197 | W | 19961220 | | |
| | US 1999-77575 | A2 | 19990119 | | |

OS MARPAT 127:126664

AB Isoquinolinesulfonyl compds. (Markush structure given) are used in ophthalmic compns. to treat glaucoma or other ischemic-borne ocular disorders such as retinopathies or optic neuropathies. These compds. vasodilate ocular blood vessels, lower intraocular pressure and prevent or reduce the progression of visual field loss. Topical administration of 150.mu.g fasudil hydrochloride (I) to rabbits eyes decreased the intraocular pressure by 14.6% after 1 h. An eye drop contain I 1.5, benzalkonium chloride 0.01, and phosphate buffered saline q.s. 100%.

IT **192712-45-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. isoquinolinesulfonyl derivs. for treatment of glaucoma and ocular ischemia)

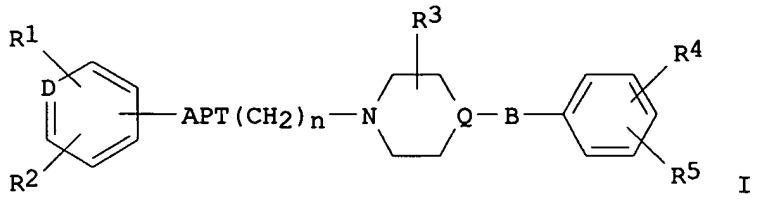
RN 192712-45-1 CAPLUS
CN 5-Isoquinolinesulfonamide, N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-(9CI) (CA INDEX NAME)



L3 ANSWER 53 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:902630 CAPLUS
DN 123:313770
TI Preparation of piperidino and piperazino 5-HT2 receptor antagonists and blood platelet aggregation inhibitors
IN Aoki, Tsuyoshi; Takahashi, Atsuo; Sato, Hiroyasu; Shimanuki, Eiji; Gengyou, Kaoru; Nishimata, Toyoki; Ishigami, Sachiko; Yamada, Shin-ichi; Yamaguchi, Takahiro; et al.
PA Toa Eiyo Ltd., Japan
SO Eur. Pat. Appl., 123 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 661266 | A1 | 19950705 | EP 1994-120698 | 19941227 |
| | R: BE, CH, DE, ES, FR, GB, IT, LI, LU, NL | | | | |
| | JP 07242629 | A2 | 19950919 | JP 1994-336707 | 19941226 |
| PRAI | JP 1993-346805 | A | 19931227 | | |

OS MARPAT 123:313770
GI

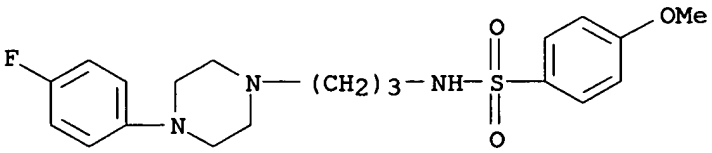


I

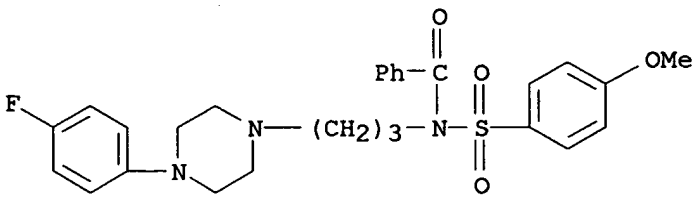
AB The title compds. [I; A = CH2, CO, sulfonyl; B, T = direct bond, CH2, CO, CH(OH), C(:NH); D = CH, N, N.fwdarw.O; P = N, N.fwdarw.O; Q = CH, N; R1, R2 = H, OH, (un)branched alkyl, alkenyl, (un)substituted aralkyl, acyl, (un)substituted NH2, etc.; R3 = H, OH, (un)branched alkyl or alkoxy; R4, R5 = H, OH, halogen, (un)branched alkyl, alkenyl, alkoxy, alkylthio, (un)substituted NH2, SH, etc.; n = 1-6], useful as 5-HT2 receptor antagonists and blood platelet aggregation inhibitors, are prepd. Thus, 4-acetylamino-N-[2-[4-(4-fluorobenzoyl)piperidino]ethyl]-N-(3-methoxyphenyl)benzamide fumarate, m.p. 215-222.degree. (decompn.), prepd. by the reaction of the free base with fumaric acid, demonstrated a IC50 for platelet aggregation in rabbit-derived, platelet-rich plasma of .ltoreq.9.9 x 10-8 M, vs. 1.0-9.9 x 10-7 M for ketanserin.

IT **169945-97-5P 169946-03-6P 169946-57-0P**
**169946-58-1P 169946-59-2P 169947-91-5P**
**169948-06-5P 169948-07-6P 169948-08-7P**
**169948-40-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidino and piperazino 5-HT2 receptor antagonists and blood platelet aggregation inhibitors)

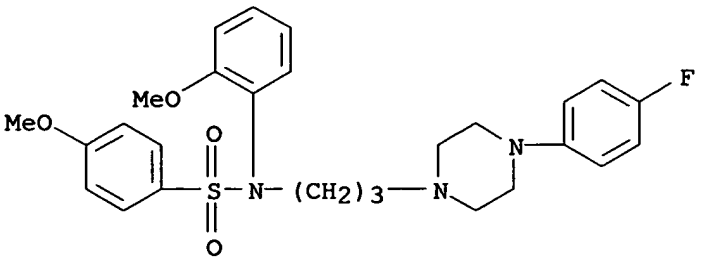
RN 169945-97-5 CAPLUS
CN Benzenesulfonamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-4-methoxy- (9CI) (CA INDEX NAME)



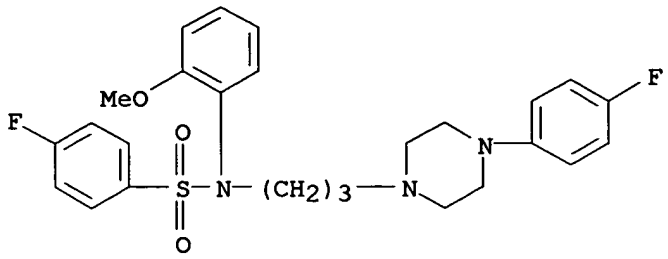
RN 169946-03-6 CAPLUS
CN Benzamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-N-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



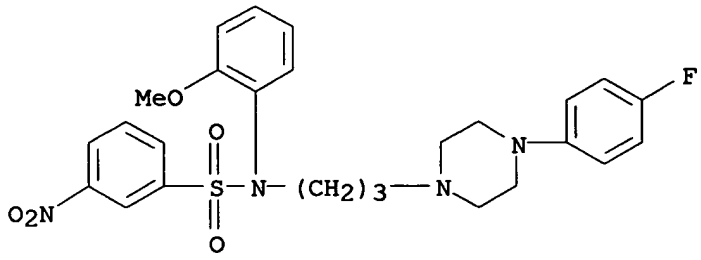
RN 169946-57-0 CAPLUS
CN Benzenesulfonamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-4-methoxy-N-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 169946-58-1 CAPLUS
CN Benzenesulfonamide, 4-fluoro-N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-N-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



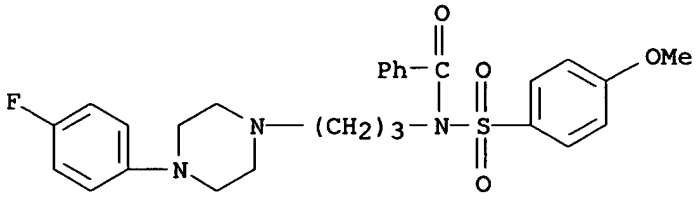
RN 169946-59-2 CAPLUS
CN Benzenesulfonamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-N-(2-methoxyphenyl)-3-nitro- (9CI) (CA INDEX NAME)



RN 169947-91-5 CAPLUS
CN Benzamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-N-[(4-methoxyphenyl)sulfonyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

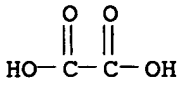
CM 1

CRN 169946-03-6
CMF C27 H30 F N3 O4 S



CM 2

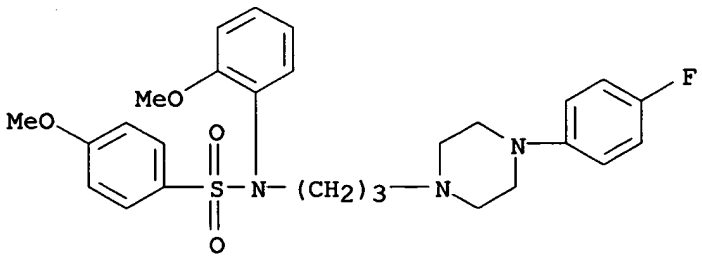
CRN 144-62-7
CMF C2 H2 O4



RN 169948-06-5 CAPLUS
CN Benzenesulfonamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-4-methoxy-N-(2-methoxyphenyl)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

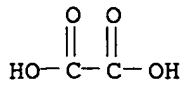
CM 1

CRN 169946-57-0
CMF C27 H32 F N3 O4 S



CM 2

CRN 144-62-7
CMF C2 H2 O4

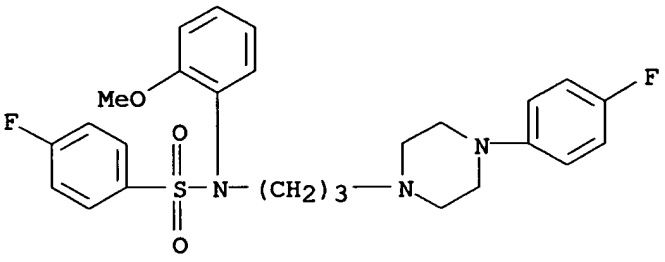


RN 169948-07-6 CAPLUS
CN Benzenesulfonamide, 4-fluoro-N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-N-(2-methoxyphenyl)-, ethanedioate (1:1) (9CI) (CA

INDEX NAME)

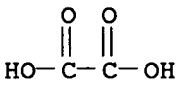
CM 1

CRN 169946-58-1
CMF C26 H29 F2 N3 O3 S



CM 2

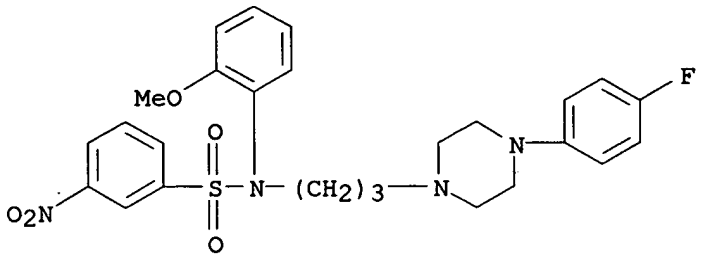
CRN 144-62-7
CMF C2 H2 O4



RN 169948-08-7 CAPLUS
CN Benzenesulfonamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-N-(2-methoxyphenyl)-3-nitro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

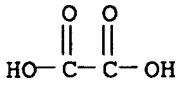
CM 1

CRN 169946-59-2
CMF C26 H29 F N4 O5 S



CM 2

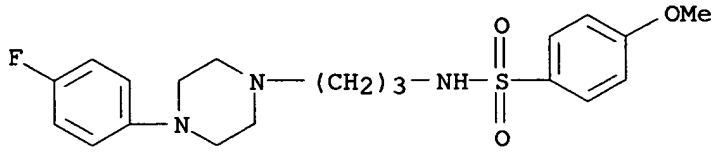
CRN 144-62-7
CMF C2 H2 O4



RN 169948-40-7 CAPLUS
CN Benzenesulfonamide, N-[3-[4-(4-fluorophenyl)-1-piperazinyl]propyl]-4-methoxy-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

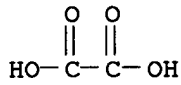
CM 1

CRN 169945-97-5
CMF C20 H26 F N3 O3 S



CM 2

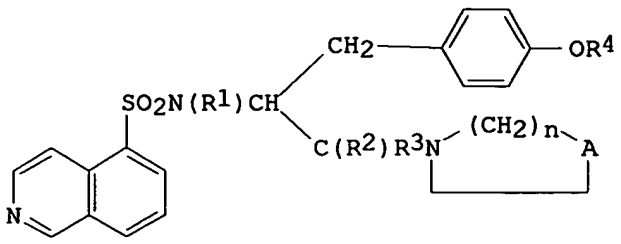
CRN 144-62-7
CMF C2 H2 O4



L3 ANSWER 60 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1993:641393 CAPLUS
DN 119:241393
TI Isoquinoline sulfonamide derivatives for anti-ulcer agents
IN Hidaka, Hiroyoshi; Ishikawa, Tomohiko
PA Japan
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5244895 | A | 19930914 | US 1992-883344 | 19920515 |
| PRAI | JP 1991-8580 | A | 19910515 | | |

OS MARPAT 119:241393
GI



I

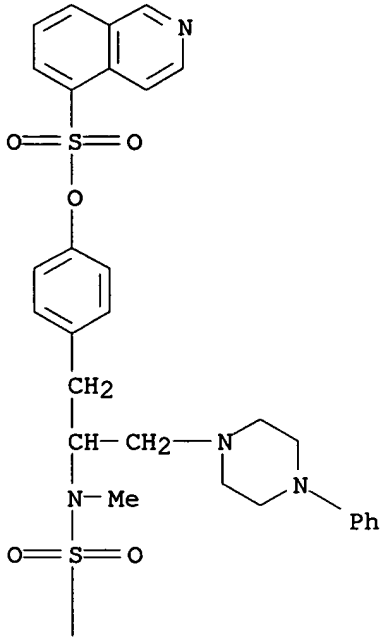
AB The anti-ulcer agents of the invention are I [R1 = H, (substituted) C1-2 alkyl; R2, R3 = H or together form oxo; R4 = H, Me, isoquinoline sulfonyl; n = 2, 3; A = NR5 CHR5 (R5 = (substituted) Ph, (substituted) benzyloxycarbonyl] or a physiol. allowable acid addn. salt thereof. Twelve specific I are claimed; and prepn. of 3 I is described. Thus, N-[N,O-bis(5-isoquinoline sulfonyl)-N-methyl-tyrosyl]-4-phenylpiperazine (II) (prepn. given) and 15 other I were tested in an anti-gastric juice secretion test and an anti-aspirin ulcer test. Tablet and injection formulations of II phosphate are included.

IT **130962-59-3 130962-61-7 130962-71-9 130962-72-0**
RL: BIOL (Biological study)
(ulcer inhibitor)

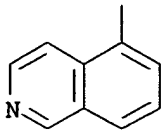
RN 130962-59-3 CAPLUS

CN 5-Isoquinolinesulfonic acid, 4-[2-[(5-isoquinolinylsulfonyl)methylamino]-3-(4-phenyl-1-piperazinyl)propyl]phenyl ester (9CI) (CA INDEX NAME)

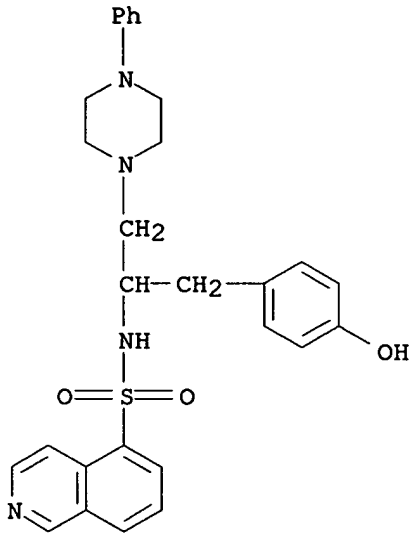
PAGE 1-A



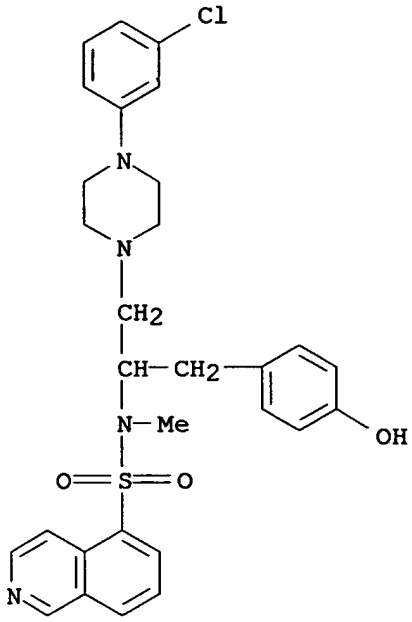
PAGE 2-A



RN 130962-61-7 CAPLUS
CN 5-Isoquinolinesulfonamide, N-[1-[(4-hydroxyphenyl)methyl]-2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

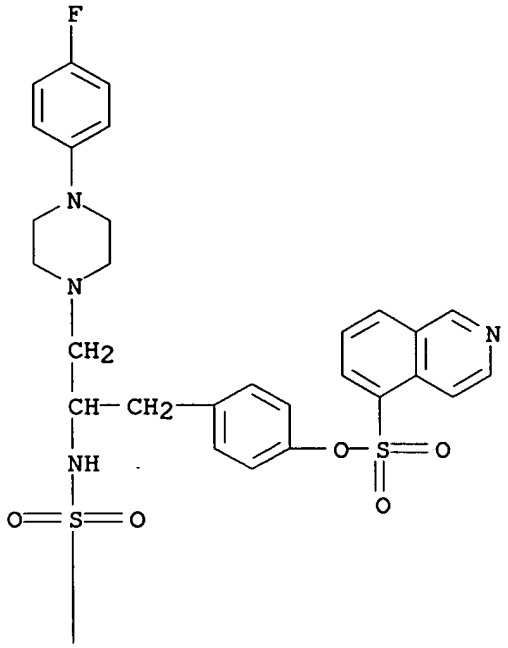


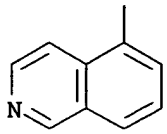
RN 130962-71-9 CAPLUS
CN 5-Isoquinolinesulfonamide, N-[2-[4-(3-chlorophenyl)-1-piperazinyl]-1-[(4-hydroxyphenyl)methyl]ethyl]-N-methyl- (9CI) (CA INDEX NAME)



RN 130962-72-0 CAPLUS
CN 5-Isoquinolinesulfonic acid, 4-[3-[4-(4-fluorophenyl)-1-piperazinyl]-2-[(5-isoquinolinylsulfonyl)amino]propyl]phenyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

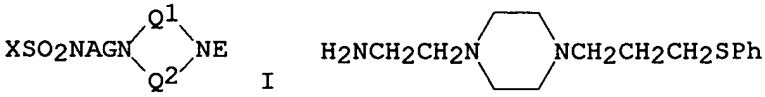




L3 ANSWER 63 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1993:80951 CAPLUS
DN 118:80951
TI Preparation of sulfonamide derivatives containing heterocyclyl groups
IN Kajihara, Akiro; Asano, Toshio
PA Asahi Kasei Kogyo K. K., Japan
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9214712 | A1 | 19920903 | WO 1992-JP146 | 19920213 |
| | W: CA, NO, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| | JP 05001037 | A2 | 19930108 | JP 1991-261394 | 19910913 |
| | CA 2089128 | AA | 19920814 | CA 1992-2080128 | 19920213 |
| | EP 525203 | A1 | 19930203 | EP 1992-904985 | 19920213 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE | | | | |
| | US 5326870 | A | 19940705 | US 1992-927493 | 19920929 |
| | NO 9203808 | A | 19921211 | NO 1992-3808 | 19920930 |
| | NO 178066 | B | 19951009 | | |
| | NO 178066 | C | 19960117 | | |
| PRAI | JP 1991-19761 | A | 19910213 | | |
| | WO 1992-JP146 | W | 19920213 | | |

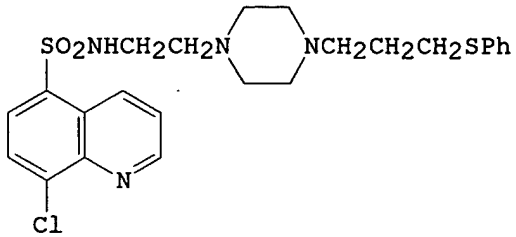
OS MARPAT 118:80951
GI



I



II



III

AB The title compds. [I; A = H, alkyl; E = alkyl, alkoxyalkyl, aryloxyalkyl, etc.; G = alkylene; Q1, Q2 = (CH2)2, (CH2)3; X = quinoline, isoquinoline,

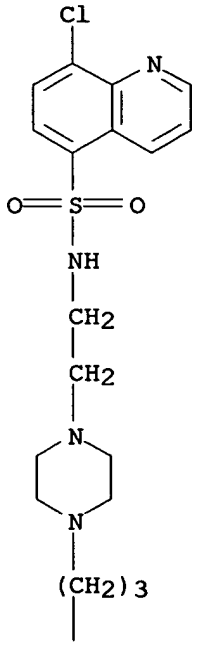
benzothiazole, 4-oxoquinazoline residue], useful as antiasthmatics, are prepd. 8-Chloro-5-quinolinesulfonic acid was refluxed with SOCl2 in DMF and the resultant sulfonyl chloride was treated with piperazine deriv. II and Et3N in CH2Cl2 at 20.degree. to give 72% sulfonamide III, which showed 82% inhibition of histamine-induced vasoconstriction at 0.1 mg/kg i.v. in guinea pigs.

IT **145708-53-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antiasthmatic agent)

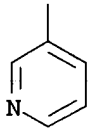
RN 145708-53-8 CAPLUS

CN 5-Quinolinesulfonamide, 8-chloro-N-[2-[4-[3-(3-pyridinyl)propyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

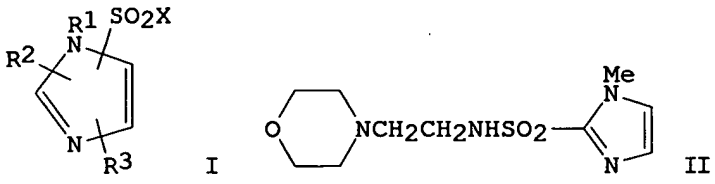


L3 ANSWER 67 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:632247 CAPLUS
DN 115:232247
TI Preparation of imidazolesulfonamides as antithrombotic agents
IN Graeve, Rolf; Okyayuz-Baklouti, Ismahan; Seiffge, Dirk
PA Hoechst A.-G., Germany

SO Ger. Offen., 39 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE 4004061 | A1 | 19910814 | DE 1990-4004061 | 19900210 |
| | EP 442348 | A2 | 19910821 | EP 1991-101497 | 19910205 |
| | EP 442348 | A3 | 19920304 | | |
| | EP 442348 | B1 | 19960717 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| | AT 140452 | E | 19960815 | AT 1991-101497 | 19910205 |
| | ES 2090150 | T3 | 19961016 | ES 1991-101497 | 19910205 |
| | FI 9100602 | A | 19910811 | FI 1991-602 | 19910207 |
| | BR 9100520 | A | 19911029 | BR 1991-520 | 19910207 |
| | CA 2035988 | AA | 19910811 | CA 1991-2035988 | 19910208 |
| | NO 9100496 | A | 19910812 | NO 1991-496 | 19910208 |
| | AU 9170848 | A1 | 19910815 | AU 1991-70848 | 19910208 |
| | AU 634342 | B2 | 19930218 | | |
| | HU 56549 | A2 | 19910930 | HU 1991-415 | 19910208 |
| | HU 207997 | B | 19930728 | | |
| | ZA 9100948 | A | 19911030 | ZA 1991-948 | 19910208 |
| | JP 04316561 | A2 | 19921106 | JP 1991-60750 | 19910208 |
| | JP 3026847 | B2 | 20000327 | | |
| | US 5232922 | A | 19930803 | US 1991-652606 | 19910208 |
| | CN 1053919 | A | 19910821 | CN 1991-100969 | 19910209 |
| | US 5356922 | A | 19941018 | US 1993-57887 | 19930507 |
| PRAI | DE 1990-4004061 | A | 19900210 | | |
| | US 1991-652606 | A3 | 19910208 | | |

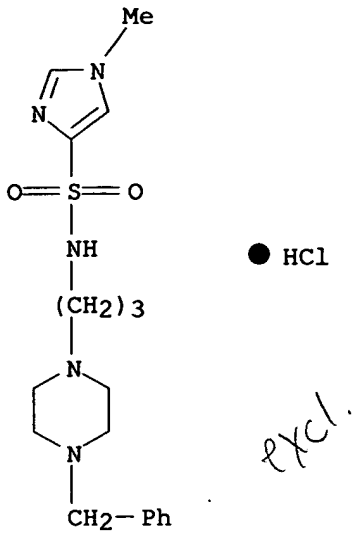
OS MARPAT 115:232247
GI




AB The title compds. [I; R1 = alkyl; R2,R3 = H, halo, alkyl; X = OH, NR4R5; R4 = H, (un)substituted alkyl; R5 = phenylalkyl, (un)substituted alkyl, etc.] were prepd. Thus, 1-methyl-2-imidazolesulfonyl chloride was condensed with 2-morpholinoethylamine to give title compd. II.HCl which gave 45% inhibition of laser-induced thromboses in rats at 10 mg/kg orally.

IT **137048-49-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antithrombotic agent)

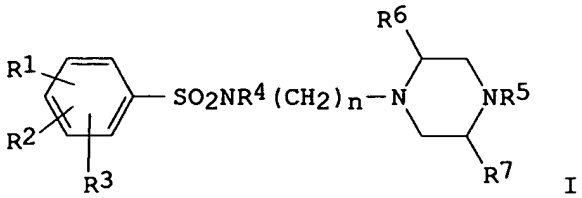
RN 137048-49-8 CAPLUS
CN 1H-Imidazole-4-sulfonamide, 1-methyl-N-[3-[4-(phenylmethyl)-1-piperazinyl]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



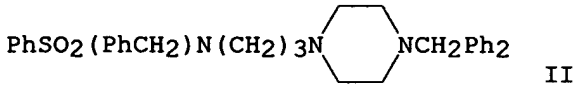

L3 ANSWER 74 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1990:98558 CAPLUS
DN 112:98558
TI Preparation and testing of N-[(arylsulfamido)alkyl]piperazines as cardiovascular agents
IN Tanabe, Sohei; Sato, Seiichi; Kyotani, Yoshinori; Ohta, Tomio; Uchida, Kasumi
PA Kowa Co., Ltd., Japan
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 330065 | A1 | 19890830 | EP 1989-102586 | 19890215 |
| | EP 330065 | B1 | 19931110 | | |
| | R: BE, CH, DE, FR, GB, IT, LI, NL, SE | | | | |
| | JP 01211567 | A2 | 19890824 | JP 1988-33949 | 19880218 |
| | JP 2556722 | B2 | 19961120 | | |
| | US 4948892 | A | 19900814 | US 1989-310684 | 19890215 |
| PRAI | JP 1988-33949 | A | 19880218 | | |

OS MARPAT 112:98558
GI



I



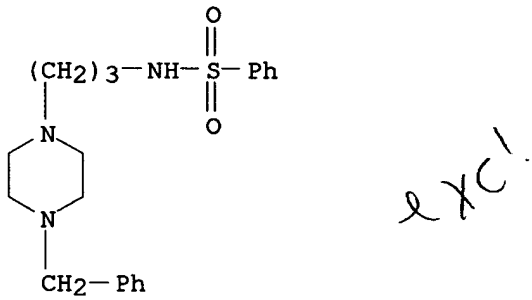
II

AB The title compds. [I; R1-R3 = H, halo, alkyl, alkoxy; R4 = H, alkyl, (substituted) aralkyl; R5 = (substituted) aryl, aralkyl; R6, R7 = H, alkyl, alkoxy; n = 1-8], useful as cardiovascular agents, were prepd. Thus, 1-diphenylmethyl-4-(3-aminopropyl)piperazine and Et3N in CH2Cl2 were treated with PhSO2Cl with ice cooling to give the sulfonamide which, in DMF, was treated with NaH and PhCH2Cl to give piperazine II. I inhibited 3,4-diaminopyridine-induced contraction of dog coronary artery rings at 10-6M. I also inhibited ADP-induced aggregation of rabbit platelet-rich plasma.

IT **125393-61-5P 125393-62-6P 125393-63-7P**
**125393-64-8P 125393-75-1P 125433-03-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as cardiovascular agent)

RN 125393-61-5 CAPLUS

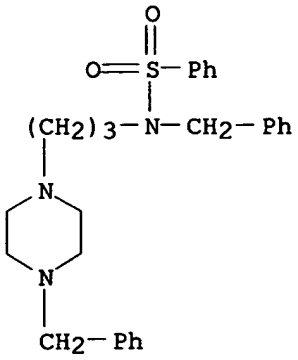
CN Benzenesulfonamide, N-[3-[4-(phenylmethyl)-1-piperazinyl]propyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

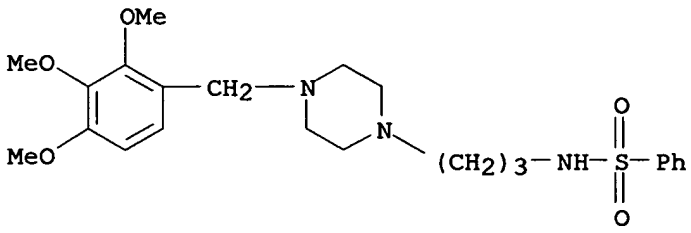
RN 125393-62-6 CAPLUS

CN Benzenesulfonamide, N-(phenylmethyl)-N-[3-[4-(phenylmethyl)-1-piperazinyl]propyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

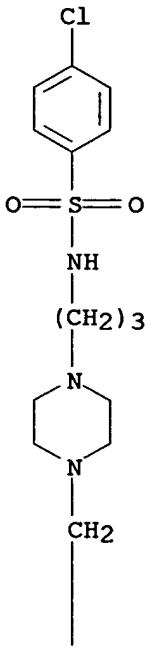
RN 125393-63-7 CAPLUS
CN Benzenesulfonamide, N-[3-[4-[(2,3,4-trimethoxyphenyl)methyl]-1-piperazinyl]propyl]-, dihydrochloride (9CI) (CA INDEX NAME)



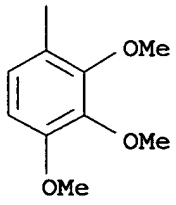
●2 HCl

RN 125393-64-8 CAPLUS
CN Benzenesulfonamide, 4-chloro-N-[3-[4-[(2,3,4-trimethoxyphenyl)methyl]-1-piperazinyl]propyl]-, dihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

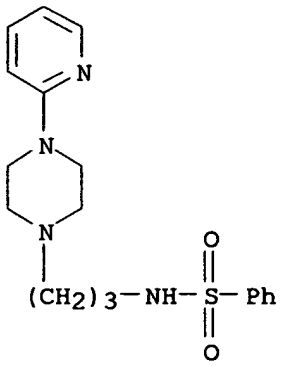


PAGE 2-A

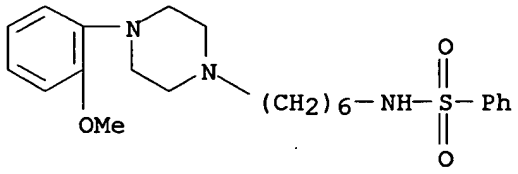


● 2 HCl

RN 125393-75-1 CAPLUS
CN Benzenesulfonamide, N-[3-[4-(2-pyridinyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



RN 125433-03-6 CAPLUS
CN Benzenesulfonamide, N-[6-[4-(2-methoxyphenyl)-1-piperazinyl]hexyl]-, dihydrochloride (9CI) (CA INDEX NAME)

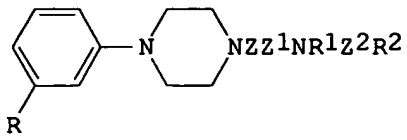


●2 HCl

L3 ANSWER 79 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1984:6557 CAPLUS
DN 100:6557
TI 1-Phenylpiperazine derivatives having antiaggressive activity
IN Van Dalen-Van der Aa, Dirkje A.; Hulkenberg, Antonius
PA Duphar International Research B. V., Neth.
SO Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | EP 89089 | A1 | 19830921 | EP 1983-200346 | 19830311 |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | DK 8301016 | A | 19830913 | DK 1983-1016 | 19830228 |
| | ES 520439 | A1 | 19840416 | ES 1983-520439 | 19830309 |
| | ZA 8301625 | A | 19841031 | ZA 1983-1625 | 19830309 |
| | AU 8312334 | A1 | 19830915 | AU 1983-12334 | 19830310 |
| | JP 58180478 | A2 | 19831021 | JP 1983-38414 | 19830310 |
| PRAI | NL 1982-1032 | A | 19820312 | | |

OS MARPAT 100:6557
GI



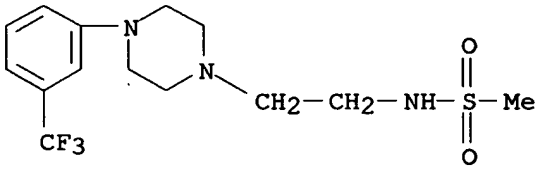
I

AB Piperazines I (R = CF3, Cl; Z = CH2, CH2CH2, CHMeCH2, CH2CHMe; Z1 = CH2, CO, SO2; R1 = H, Me, Et; Z2 = CO, SO2; R2 = NH2, alkylamino, dialkylamino, alkyl, cyclohexyl, cyclohexylmethyl, cyclohexyloxymethyl, benzyl, thenyl, pyridylmethyl, PhOCH2, PhSCH2, a 1-phenylcycloalkyl group, alkoxy, cycloalkyloxy, aralkoxy), useful as anti-aggressive agents (no data), were prepd. Thus, a mixt. of ClCH2CH2CONHSO2NH2, 1-[3-(trifluoromethyl)phenyl]piperazine, and Et3N in THF was refluxed to give I (R = CF3, Z = CH2CH2, Z1 = CO, R1 = H, Z2 = SO2, R2 = NH2).

IT **88069-02-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 88069-02-7 CAPLUS

CN Methanesulfonamide, N-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L3 ANSWER 83 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1969:87765 CAPLUS

DN 70:87765

TI Sedative, antiadrenergic, and hypotensive 2-substituted 2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxides

AU Hayao, Shin; Strycker, W. G.; Phillips, B. M.; Fujimori, H.; Vidrio, H.

CS Ther. Res. Div., Miles Lab., Inc., Elkhart, IN, USA

SO Journal of Medicinal Chemistry (1968), 11, 1246-8
CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

GI For diagram(s), see printed CA Issue.

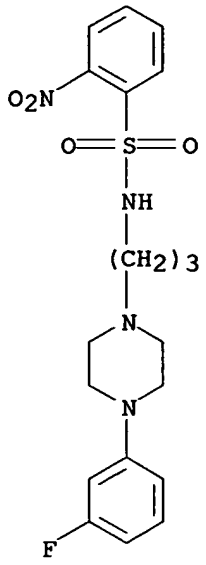
AB Treatment of o-nitro-benzenesulfonyl chloride with amines gave o-nitrobenzenesulfon-amides which were hydrogenated to o-aminobenzenesulfonamides which were cyclized by treatment with COCl2 in boiling PhCl to give 2-substituted 2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxides. Similarly, o-aminobenzenesulfonamide was cyclized with urea at 200.degree. or with COCl2 in boiling PhCl to give unsubstituted 2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide, which was alkylated to give 2-substituted compds. An ice-cold soln. of 55 g. 1-(3-aminopropyl)-4-(m-fluorophenyl)piperazine in 150 ml. C6H6 and 100 ml. 20% NaOH soln. was treated with a soln. of 51.3 g. o-nitrobenzenesulfonyl chloride in 150 ml. C6H6 and the reaction mixt. stirred 2 hrs. at 25.degree., acidified with dil. HCl, and made basic with NH4OH to give

78.8 g 4-(m-fluorophenyl)-1-[3-(o-nitrobenzenesulfonamido)propyl]piperazin e (I) m. 111-12.degree. (C6H6-hexane). A soln. of 77.5 g. I in 210 ml. HOAc was hydrogenated over 5 g. 10% Pd/C to give 65.2 g. 1-[3-(o-amino-benzenesulfonamido)propyl]-4-(m-fluorophenyl)piperazine (II), m. 119-20.degree. (C6H6-hexane and MeOH). To an ice-cold soln. of 250 ml. PhCl contg. 50.9 g. COCl2 was added 44.4 g. II and the suspension refluxed 1 hr. to give 39.0 g. 2-[3-(4-m-fluorophenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide (III) hydrochloride, m. 257-8.degree. (decompn.) (MeOH- HCONMe2). The combined filtrates were concd. in vacuo and made basic with NH4OH to give 12.4 g. III, m. 148-9.degree. (MeOH). A soln. of 34.1 g. 6-chloro-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide and 23.8 g. NaOMe in 200 ml. abs. EtOH and 100 ml. Me2SO was treated with 45.4 g. 1-(3-chloropropyl)-4-phenylpiperazine dihydrochloride and refluxed 20 hrs. The soln. was filtered and the filtrate concd. in vacuo and worked up to give 14.0 g. 6-chloro-2-[3-(4-phenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide hydrochloride (IV), m. 227-9.degree. (decompn.); free base m. 152-3.degree. (aq. MeOH-HCONMe2). V prepd. were (n, Q, m.p., and m.p. HCl salt given): 3, 4-phenyl-1-piperazinyl, 152-3.degree., 256-7.degree. (decompn.); 3, 4-(m-chlorophenyl)-1-piperazinyl, 149-50.degree., 224-6.degree. (decompn.); 3, 4-(m-trifluoromethylphenyl)-1-piperazinyl, 158-9.degree., 262-3.degree. (decompn.); 3, 4-(p-fluorophenyl)-1-piperazinyl, 165-7.degree., 228-30.degree.; 3, 4-phenyl-1-piperidinyl, 161-2.degree., 219-20.degree. (decompn.); 4, 4-(m-chlorophenyl)-1-piperazinyl, 161-3.degree. (decompn.), -; 5, 4-phenyl-1-piperazinyl, 190.degree. (decompn.), -. In exptl. animals, the activity of 2-[3-(4-p-fluorophenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiodiazin-3(4H)-one 1,1-dioxide hydrochloride (VI) as a psychosedative was comparable to that of chlorpromazine and 3-[3-(4-m-chlorophenyl-1-piperazinyl)propyl]-2,4(1H,3H)-quinazolinedione hydrochloride. Except for VI, the compds. showed weaker sedative and hypotensive activities than the corresponding 3-substituted 2,4(1H,3H)-quinazolinediones. Studies of the antiadrenergic and hypotensive activities indicated that the unsubstituted phenylpiperazine and phenylpiperidine derivs. had greater activity than compns. with substituents in the Ph ring. The compds. produced a small decrease in the water and electrolyte excretion in rats.

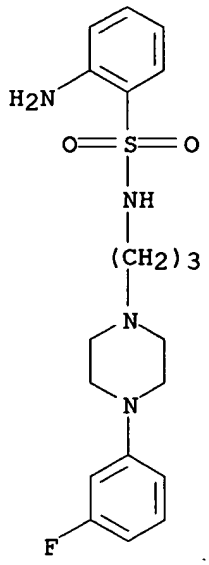
IT **21920-27-4P 21920-28-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 21920-27-4 CAPLUS

CN Benzenesulfonamide, N-[3-[4-(m-fluorophenyl)-1-piperazinyl]propyl]-o-nitro- (8CI) (CA INDEX NAME)



RN 21920-28-5 CAPLUS
CN Benzenesulfonamide, o-amino-N-[3-[4-(m-fluorophenyl)-1-piperazinyl]propyl]- (8CI) (CA INDEX NAME)



L3 ANSWER 84 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1967:10968 CAPLUS
DN 66:10968
TI 2H-1,2,4-Benzothiadiazine-3(4H)-one 1,1-dioxide derivatives
IN Hayao, Shin
PA Miles Laboratories, Inc.
SO U.S., 6 pp.

CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 3267096 | | 19660816 | US | 19650224 |

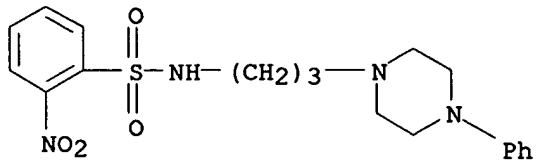
GI For diagram(s), see printed CA Issue.

AB The title compds. are useful as central as central nervous system depressants, antiinflammatory agents, and antihypertensive agents and were prepd. according to the given scheme (n = 3 to 5 and X is H F, Cl, or F3C). Thus, to an ice cold soln. of 43.8 1-(3-aminopropyl)-4-phenylpiperazine in 100 ml. C6H6 and 100 ml. 20% NaOH was added with vigorous stirring a soln. of 44.3 g. o-O2NC6H4SO2Cl in 100 ml. C6H6. The brown cloudy soln. was stirred an hr. and acidified with dil. HCl soln. to give a gummy mixt., which was made basic with NH4OH to give a light yellow solid. After filtration, the solid was washed with H2O and Et2O and dried at 50.degree. to give 98% N-[3-(4-phenyl-1-piperazinyl)-propyl]-2-nitrobenzenesulfonamide (I), m. 175.degree. (softens at 135.degree.); recrystd. product m. 138-9.degree. [aq. MeOH-HCONMe2 (DMF)], yield 24.9 g. A soln. of 23.9 g. I in 200 ml. HOAc was reduced over 5 g. freshly prepd. 5% Pd-C with shaking overnight. The mixt. was filtered, the solvent removed, the residual sirup cooled in an ice-H2O bath, and basified with concd. NH4OH soln., and the gracy oil taken into CHCl3-Et2O and dried over MgSO4. A satd. soln. of HCl in iso-PrOH, (200 ml.) was added and the product isolated (24.9 g.) was the HCl salt of 2-amino-N-[3-(4-phenyl-1-piperazinyl)propyl]benzenesulfonamide, m. 226-8.degree.; the free base (II), m. 117-18.degree.. A slow stream of COCl2 was bubbled 60 min. into a boiling soln. of 31.3 g. II in 250 ml. ClPh, the mixt. cooled, and the solid product collected, washed with EtOAc-Et2O and H2O, and air-dried to give 38.2 g. product, m. 226-32.degree.. The product was titurated with aq. NH4OH to yield 35.2 g. 2-[3-4(-phenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiazin-3(4H)-one 1,1-dioxide (III), m. 151-4.degree. (aq. Me2CO). III was dissolved in hot MeOH satd. with HCl to give 26.6 g. III.HCl.-MeOH, m. 256-7.degree.. By a similar sequence of reactions, 76.1 g. 2-nitro-N-[3-(4-m-chlorophenyl-1-piperazinyl)propyl]benzenesulfonamide gave 75.8 g. 2-amino-N-[3-(4-m-chlorophenyl-1-piperazinyl)propyl]benzenesulfonamide-HCl.MeOH (IV), m. 155-6.degree. (decompn.) (methanolic HCl-EtOAc). The HCl salt was suspended in H2O, aq. NH4OH added, the orange-yellow gum extd. with CHCl3 to yield 54.8 g. of the free base of IV, m. 105-7.degree.. Reaction with COCl2 in ClPh gave 47.4 g. 2-[3-(4-m-chlorophenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiazin-3(4H)-one 1,1-dioxide-HCl (V), m. 224-6.degree. (aq. MeOH-DMF). The free base of V (9.5 g.), m. 149-50.degree., was isolated from the filtrate. Likewise, 44 g. 1-m-chlorophenyl-4-(4-aminobutyl)piperazine was converted to 2-nitro-N-[4-m-chlorophenyl-1-piperazinyl)butyl]benzene sulfonamide. Redn. yielded 67.6 g. of the HCl salt of 2-amino-N-[4-(4-m-chlorophenyl-1-piperazinyl)butyl]benzenesulfonamide which is converted to the free base on treatment with aq. NH4OH. The free base (51.4 g.) was allowed to react with COCl2 to give 44.9 g. 2-[4-(4-m-chlorophenyl-1-piperazinyl)butyl]-2H-1,2,4-benzothiazin-3(4H)-one 1,1-dioxide-HCl (VI), m. 210-16.degree. (decompn.), which on treatment with aq. NH4OH yielded 29.1 g. the free base of VI, m. 133-4.degree., and this base was converted to 33.1 g. of the maleic acid salt, m. 161-3.degree. (decompn.) (EtOAc). The reaction of COCl2 in ClPh with 76 g. 2-amino-N-[3-(4-m-trifluoromethylphenyl-1-piperazinyl)propyl]benzenesulfonamide gave a product which was dissolved in Et2O and treated with maleic acid to give 91.7 g., m. 173-83.degree. (decompn.), of a crude maleate. It was converted to the free base to give

45 g. 2-[3-(4-m-trifluoro-methylphenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide (VII), m. 141-53.degree. (aq. MeOH). The VII obtained and maleic acid in MeOH gave 28.4 g. VII.C4H4O4, m. 184-5.degree. (MeOH-Et2O), and was converted to 10.7 g. VII.HCl, m. 262-3.degree. (decompn.). 1-(Aminopropyl)-4-phenylpiperidine (40.1 g.) was converted to 59.4 g. 2-nitro-N-[3-(4-phenyl-1-piperidinyl)propyl]benzenesulfonamide (VIII), m. 113-14.degree. (aq. MeOH). Redn. of the nitro group in VIII to an amino group, followed by the treatment with COCl2 in ClC6H5 gave 20.8 g. 2-[3-(4-phenyl-1-piperidinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide-HCl.MeOH (IX), m. 219-20.degree. (aq. MeOH). Addn. of aq. NH4OH to the filtrates of the crystn. liquors gave 16 g. of the free base of IX, m. 161-2.degree. (aq. Me2CO). 2-Nitro-N-[5-(4-phenyl-1-piperazinyl)pentyl]benzenesulfonamide (X) (77%), m. 128-30.degree. (aq. MeOH-DMF), was obtained from 1-(5-aminopentyl)-4-phenylpiperazine. Redn. of 74.3 g. X with H in the presence of Pd-C gave 54.2 g. 2-amino-N-[5-(4-phenyl-1-piperazinyl)pentyl]benzenesulfonamide, m. 152-3.degree. (Me2CO-CHCl3-n-C6H14), of which 52.9 g. was converted to 22.2 g. 2-[5-(4-phenyl-1-piperazinyl)pentyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide-2HCl, m. 190.degree. (decompd. 175.degree.) (MeOH contg. HCl). 1-(3-Aminopropyl)-4-fluorophenylpiperazine (35.6 g.) gave 40.3 g. 2-nitro-N-[3-(4-p-fluorophenyl-1-piperazinyl)propyl]benzenesulfonamide, m. 132-3.degree. (Me2CO-MeOH-n-C6H14), of which 39 g. was reduced to yield 34.2 g. of 2-amino-N-[3-(4-p-fluorophenyl)propyl]benzenesulfonamide, m. 121-2.degree. (aq. MeOH), and 40 g. of this compd. was treated with COCl2 to yield 30.2 g. of 2-[3-(4-p-fluorophenyl-1-piperazinyl)propyl]-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide-HCl, m. 228-230.degree. (aq. MeOH-EtOAc). Spectral data are included in the analytical results for the new compds.

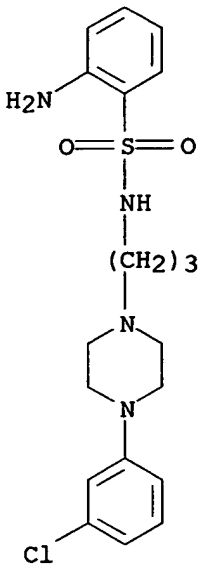
IT **13349-02-5P 13349-05-8P 13349-06-9P 13530-43-3P 13530-44-4P 13530-46-6P 13530-47-7P 13559-86-9P 13631-18-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 13349-02-5 CAPLUS
CN Benzenesulfonamide, o-nitro-N-[3-(4-phenyl-1-piperazinyl)propyl]- (8CI) (CA INDEX NAME)



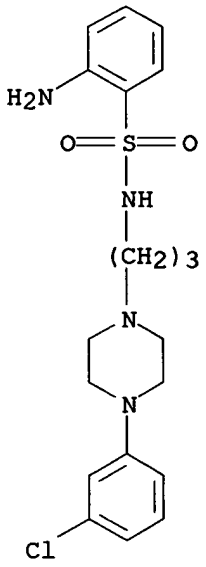

exc!.

RN 13349-05-8 CAPLUS
CN Benzenesulfonamide, o-amino-N-[3-[4-(m-chlorophenyl)-1-piperazinyl]propyl]-, trihydrochloride (8CI) (CA INDEX NAME)

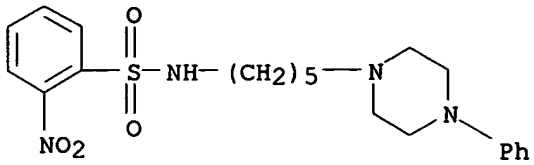


● 3 HCl

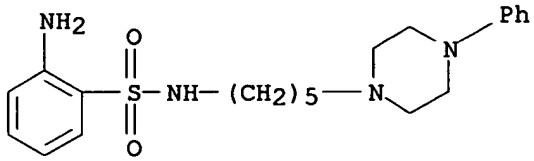
RN 13349-06-9 CAPLUS
CN Benzenesulfonamide, o-amino-N-[3-[4-(m-chlorophenyl)-1-piperazinyl]propyl]- (8CI) (CA INDEX NAME)



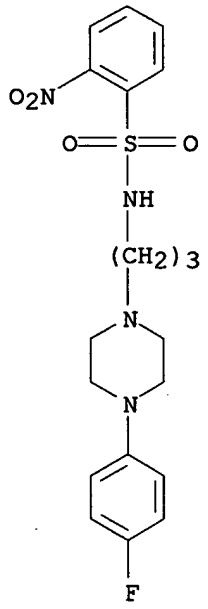
RN 13530-43-3 CAPLUS
CN Benzenesulfonamide, o-nitro-N-[5-(4-phenyl-1-piperazinyl)pentyl]- (8CI) (CA INDEX NAME)



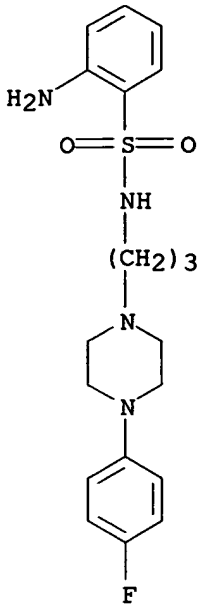
RN 13530-44-4 CAPLUS
CN Benzenesulfonamide, o-amino-N-[5-(4-phenyl-1-piperazinyl)pentyl]- (8CI) (CA INDEX NAME)



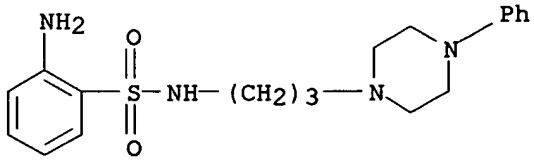
RN 13530-46-6 CAPLUS
CN Benzenesulfonamide, N-[3-[4-(p-fluorophenyl)-1-piperazinyl]propyl]-o-nitro- (8CI) (CA INDEX NAME)



RN 13530-47-7 CAPLUS
CN Benzenesulfonamide, o-amino-N-[3-[4-(p-fluorophenyl)-1-piperazinyl]propyl]- (8CI) (CA INDEX NAME)

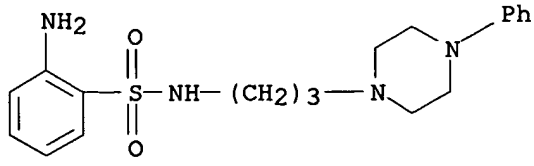


RN 13559-86-9 CAPLUS
CN Benzenesulfonamide, o-amino-N-[3-(4-phenyl-1-piperazinyl)propyl]-, dihydrochloride (8CI) (CA INDEX NAME)



●2 HCl

RN 13631-18-0 CAPLUS
CN Benzenesulfonamide, o-amino-N-[3-(4-phenyl-1-piperazinyl)propyl]- (8CI) (CA INDEX NAME)

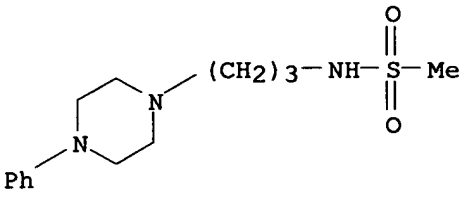


L3 ANSWER 85 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1956:32338 CAPLUS
DN 50:32338

OREF 50:6522c-d
TI Phenyl-substituted piperazine compounds
IN Fleming, Robert W.; Parcell, Robert F.
PA Parke, Davis & Co.
DT Patent
LA Unavailable
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2722529 | | 19551101 | US | |

AB See Brit. 721,417 (C.A. 50, 2683i).
IT **500797-20-6**, Methanesulfonamide, N-[3-(4-phenyl-1-piperazinyl)propyl]-
(prepn. of)
RN 500797-20-6 CAPLUS
CN Methanesulfonamide, N-[3-(4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



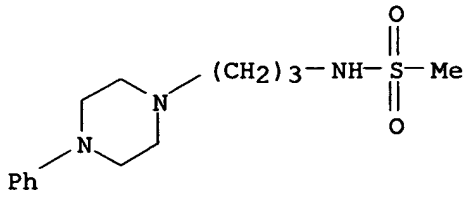
L3 ANSWER 86 OF 86 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1956:12597 CAPLUS
DN 50:12597
OREF 50:2683i,2684a-b
TI Phenyl substituted piperazine compounds
PA Parke, Davis & Co.
DT Patent
LA Unavailable
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 721417 | | 19550105 | GB | |

GI For diagram(s), see printed CA Issue.
AB In this abstr. R = CH2.CH2.NPh.CH2.CH2.N. RCH2CH2CH2NH2 (21.9 g.) and 100 cc. EtO2CH is heated under reflux for 2 h., the excess ester removed by distn. and the residue recrystd. from C6H6 and petr. ether to yield 8 g. RCH2CH2CH2NHCOH, m. 100-1.degree.. The following compds. are also described: RCH2CH2CH2NHCOCHCl2, m. 81-2.degree.; RCH2CH2CH2NHSO2Me (I), m. 105-7.degree.; I.HBr salt, m. 172-4.degree.; RCH2CH2CH2NHBz, m. 109-10.degree.; R(CH2)6NHCOH, m. 65-7.degree.; R(CH2)3NHAc, m. 100-2.degree.; R(CH2)3NHCONH2, m. 146-8.degree.; RCH2CHMeNHAc, m. 96-8.degree.; R(CH2)3NHCOR' (R' = cyclohexyl), m. 112-14.degree.; R(CH2)3NHCO(CH2)5R', m. 90-1.degree.; R(CH2)2NHCOCH2Ph, m. 127-9.degree.; RCH2CH2NHCOH, m. 95-6.degree.; RCH2CH2NHAc, m. 105-7.degree.; R(CH2)3NHCOEt, m. 81-2.degree.; R(CH2)4NHtAc, m. 107-8.degree.; R(CH2)5NHAc, m. 86-7.degree.; R(CH2)4NHSO2Me, m. 80-1.degree.; R(CH2)5NHSO2Me, m. 103-5.degree..
IT **500797-20-6**, Methanesulfonamide, N-[3-(4-phenyl-1-piperazinyl)propyl]-

same as 85

(prepn. of)
RN 500797-20-6 CAPLUS
CN Methanesulfonamide, N-[3-(4-phenyl-1-piperazinyl)propyl]- (9CI) (CA INDEX NAME)



=> log h

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 87.79 | 99.44 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -12.75 | -12.75 |

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:17:30 ON 29 JAN 2006